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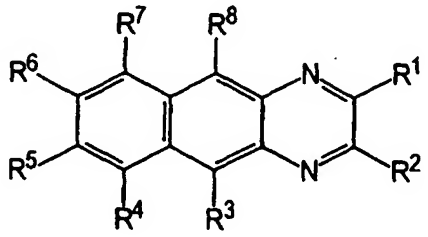
(54) Title: BENZO[G]QUINOXALINE DERIVATIVES AS EFFECTIVE COMPOUNDS AGAINST INFECTIOUS DISEASES



(I)

(57) Abstract: The present invention relates to benzo[g]quinoxaline derivatives of the general formula (I), processes for manufacturing said benzo[g]quinoxaline derivatives, the use of the benzo[g]quinoxaline derivatives as pharmaceutically active agents, especially for the prophylaxis and/or treatment of infectious diseases and opportunistic infections, diabetes, cancer, inflammation, as well as compositions containing at least one benzo[g]quinoxaline derivative and/or pharmaceutically acceptable salt thereof. Further, the present invention is directed to methods for preventing and/or treating of infectious diseases, diabetes, cancer, and inflammation using the inventive benzo[g]quinoxaline derivatives.

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Benzo[g]quinoxaline derivatives as effective compounds against infectious diseases

Specification

The present invention relates to benzo[g]quinoxaline derivatives, processes for manufacturing said benzo[g]quinoxaline derivatives, the use of the benzo[g]quinoxaline derivatives as pharmaceutically active agents, especially for the prophylaxis and/or treatment of infectious diseases and opportunistic infections, diabetes, cancer, inflammation, as well as compositions containing at least one benzo[g]quinoxaline derivative and/or pharmaceutically acceptable salt thereof. Furthermore, the present invention is directed to methods for preventing and/or treating of infectious diseases, diabetes, cancer, and inflammation as well as other TNFα mediated diseases using the inventive benzo[g]quinoxaline derivatives.

Mycobacteria:

Mycobacteria are the causative agents of tuberculosis, leprosy and mycobacteria-induced meningitis. They are divided in different groups by their ability to generate symptomatic diseases. For example members of the 'Avium'-complex of mycobacteria (i.e. *M. tuberculosis*, *M. avium*, *M. bovis*, *M. africanum* and *M. microti*) induce the severe and in many cases fatal disease tuberculosis. Tuberculosis usually affects the lungs, although in up to one-third of cases other organs are involved. If untreated, the disease may be fatal within five years in more than half of the cases. 90 million new cases and 30 million deaths due to tuberculosis have been reported during the 1990s. Leprosy (Hansen's disease) is caused by *M. leprae*. Therapy for leprosy still remains difficult, especially in developing countries, because of the long duration and high cost of therapy required, the frequency of adverse reactions to drugs, the acquisition of drug resistance, the difficulty of determining a disease end point or cure, and given that *M. leprae* still cannot be grown in vitro, the difficulty of conducting susceptible testing. Although less pathogenic than *M. tuberculosis* the nontuberculous mycobacteria can cause pulmonary, skin, bone and joint, lymph node and soft tissue infections as well as disseminated disease in immunocompromised hosts, including patients with AIDS and other immunodeficiencies. Up to 40% of AIDS patients develop disseminated disease with *Mycobacterium avium-intracellulare* (MAI). Infections due to *M.*

haemophilum occur most commonly as disseminated disease in immunocompromised patients with and without AIDS. For instance, tuberculosis is an important opportunistic disease among HIV-infected persons worldwide. In some developing countries of Africa, Southeast Asia and Latin America, an estimated amount of 8.5 million persons were coinfected as of the middle of 1996. HIV of AIDS patients directly attacks the critical immune mechanisms involved in protection against tuberculosis so that tuberculosis can appear at any stage of HIV infection. Mycobacteremia and meningitis also occur particularly during advanced HIV diseases. In the United States of America *M. xenopi* most often causes nosocomial infections. These infections most commonly occur in the environment of the hospital's hot-water systems. *M. genavense* is a newly recognized organism that grows only in liquid media. This organism almost exclusively infects AIDS patients, causing disseminated disease.

AIDS and HIV:

With respect to the numbers of HIV-infected individuals, each day about 16,000 people worldwide are infected with the virus, with 95% of new cases occurring in developing countries (mostly Africa). More than 2.6 million people died of AIDS in 1999 alone, the highest reported number since data gathering about the disease began in the early 1980s. According to the American Medical Association, about 45 million people worldwide are infected with HIV. Of the more than 2.6 million people died of AIDS-associated diseases in 1999, an estimated 550,000 were children under 15 years of age. Although life expectancy increased very significantly by introduction of new treatments, at the present time no cure exists for AIDS.

Hepatitis B Virus (HBV):

Hepatitis is an inflammation of the liver that is most often caused by infection with one of five viruses, hepatitis A, B, C, D or E. In cases, particularly in those related to hepatitis B and C, "chronic hepatitis" may result. Chronic hepatitis occurs when the body is unable to completely clear the virus even though the symptoms may not persist. Continued presence of the virus over a number of years can lead to cirrhosis (scarring of the liver) or hepatocellular carcinoma (liver cancer). HBV is transmitted through sexual contact, vertical transmission (mother to child at birth) or by coming into contact with contaminated blood. It is estimated that over 2 billion people worldwide have been infected with hepatitis B virus. Of these 2 billion, approximately 350 million people have developed chronic HBV infection, putting them at high risk of developing cirrhosis and liver

cancer (World Health Organization Fact Sheet on Hepatitis B, Nov. 1998). According to the CDC (fact sheet Sept. 00), 140,000-320,000 infections occur per year in the United States, an estimated 1-1.25 million Americans are chronically infected and the estimated costs in medical and work loss in the United States come to $700 million per year (1991).

Chronic carriers of HBV have been defined as those who are HBV surface antigen positive for more than 6 months. Approximately 5-10% of those adults who are infected with the virus will become carriers, an estimated 5-10% of those people infected each year will progress to chronic liver disease, cirrhosis and possibly liver cancer. About 5,000 people die in the United States each year related to Hepatitis B, 1,000 die of HBV-related liver cancer.

The incubation period of HBV usually lasts from 2 to 4 months, although it may be very short (10 days) or extremely long (9 months). Before the outbreak of the acute disease HBs- and HBe-antigen are detectable in the patient's serum. The onset of acute hepatitis is characterized by the occurrence of anti-HBc antibodies which at first exclusively belong to the IgM class. From this time on anti-HBc antibodies will be detectable in the patient's serum for the rest of his life, no matter whether there is an acute hepatitis B, a form of persisting virus infection or some naturally acquired immunity to HBV.

The most significant event indicating a chronic course of hepatitis B is the absence of the HBsAg/anti-HBs seroconversion. If this phenomenon has not occurred within 6 months after the onset of the disease, persistence of the HBV infection and the related clinical pictures (asymptomatic HBsAg carrier, chronic liver disease, cirrhosis, or hepatoma) have to be reckoned with.

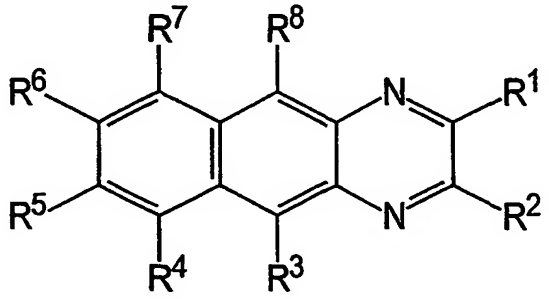
While there are effective vaccines for the prevention of HBV infection, the treatments available to those who become infected are not satisfactory. Current treatments focusing on compounds like lamivudine (e.g., Epivir-HBV) or cytokines like interferon-alfa2b (e.g. Intron A) show some benefits for chronic hepatitis B, but there is clearly a need for additional therapies.

It is object of the present invention to provide a novel compound class which can be used as pharmaceutically active agents, especially for prophylaxis and/or treatment of infectious diseases, diabetes, cancer, inflammation and TNFα mediated diseases, methods wherein said members of said compound class are

used in order to treat infectious diseases, diabetes, cancer, inflammation and TNFα mediated diseases and compositions containing at least one inventive compound and/or pharmaceutically acceptable salt thereof as a pharmaceutically active ingredient.

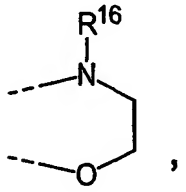
The object of the present invention is solved by the teaching of the independent claims. Further advantageous features, aspects and details of the invention are evident from the dependent claims, the description, the figures, and the examples of the present application.

One aspect of the present invention is related to compounds of the general formula (I):



wherein:

R^1 and R^2 are independently of each other $-(CH_2)_p-NH-(CH_2)_n-R^9$, $-(CH_2)_s-S-(CH_2)_m-R^{10}$, $-(CH_2)_m-O-(CH_2)_p-R^{11}$, $-(CH_2)_r-R^3$, $-CH=CH-R^{11}$, $-(CH_2)_m-CH(OH)-(CH_2)_p-R^{11}$, $-(CH_2)_q-R^{11}$, $-R^9$, $-R^{10}$, $-R^{12}$, $-R^{13}$,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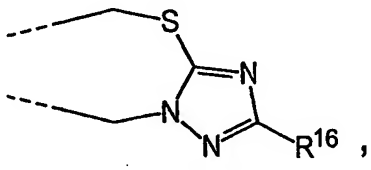
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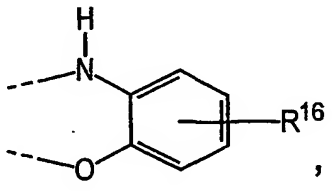
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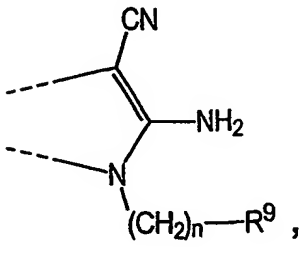
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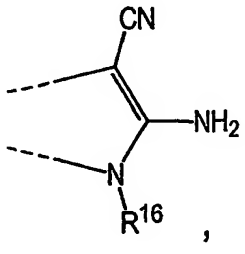
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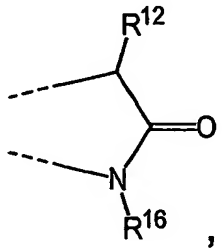
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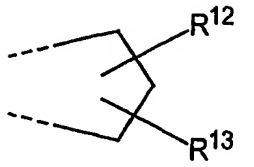
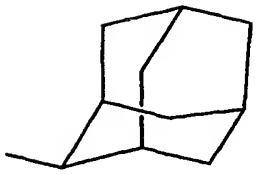
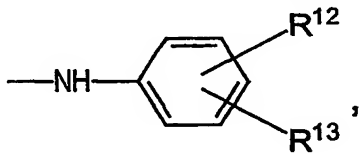
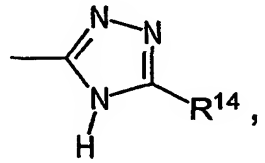
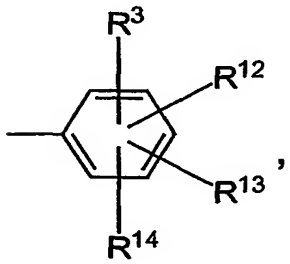
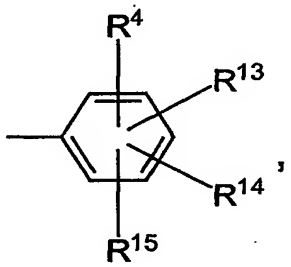
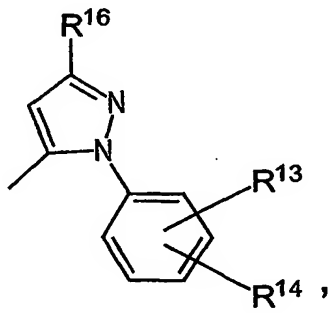
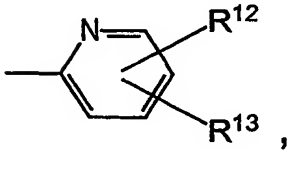
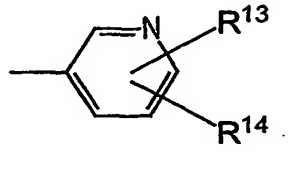
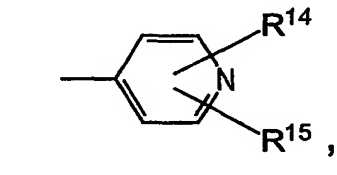



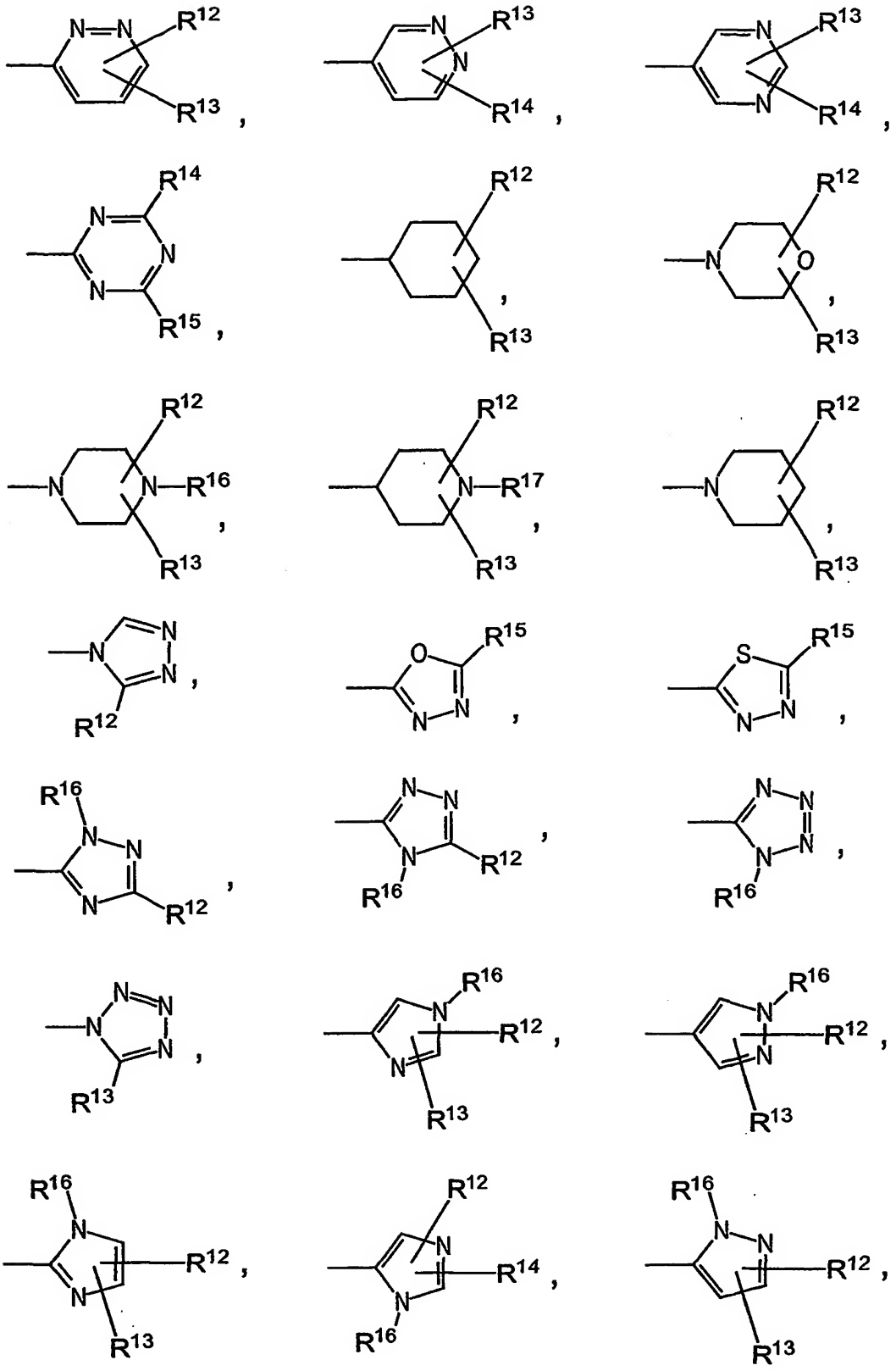
R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other —H, —F, —Cl, —Br, —I, —SO_3H, —SO_3NH_2, —$(CH_2)_s$–$COOR^{16}$, —$(CH_2)_p$–$COOR^{17}$, —OR^{16}, —SR^{16}, —$NR^{16}R^{17}$, —$OOCR^{16}$, —$OOCR^{17}$, —NH–CO–R^{16}, —NH–CO–R^{17}, —CO–NH–R^{16}, —CO–NH–R^{17}, —NO_2, —N_3, —CN, —OCN, —NCO, —SCN, —NCS, —CO–R^{16}, —CO–R^{17}, —COCN, —$CONR^{16}R^{17}$, —SOR^{16}, —SOR^{17}, —SO_2R^{16}, —SO_2R^{17}, —SO_3R^{16}, —SO_3R^{17}, —OCF_3;

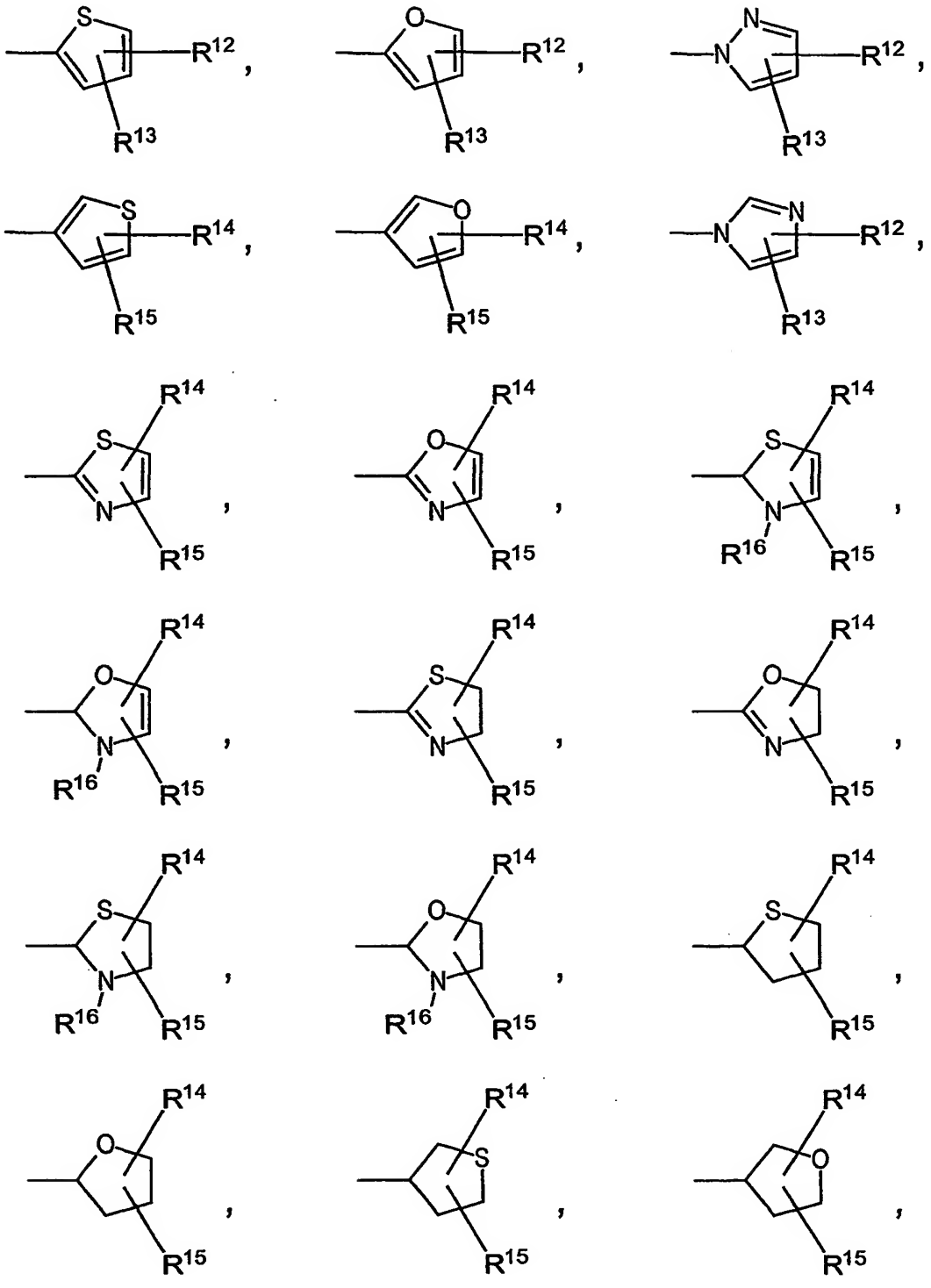
R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$, —NHR^{16},

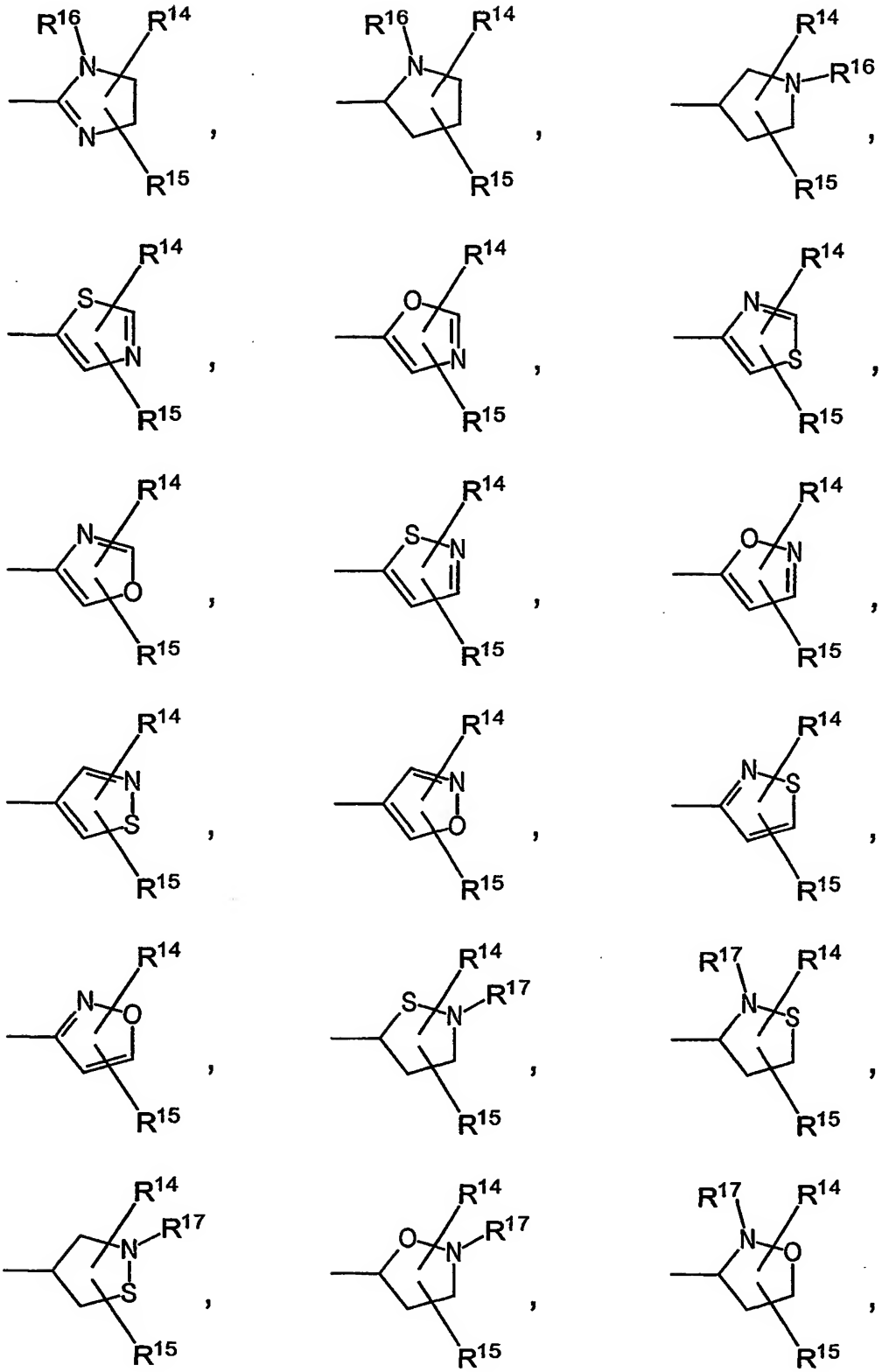



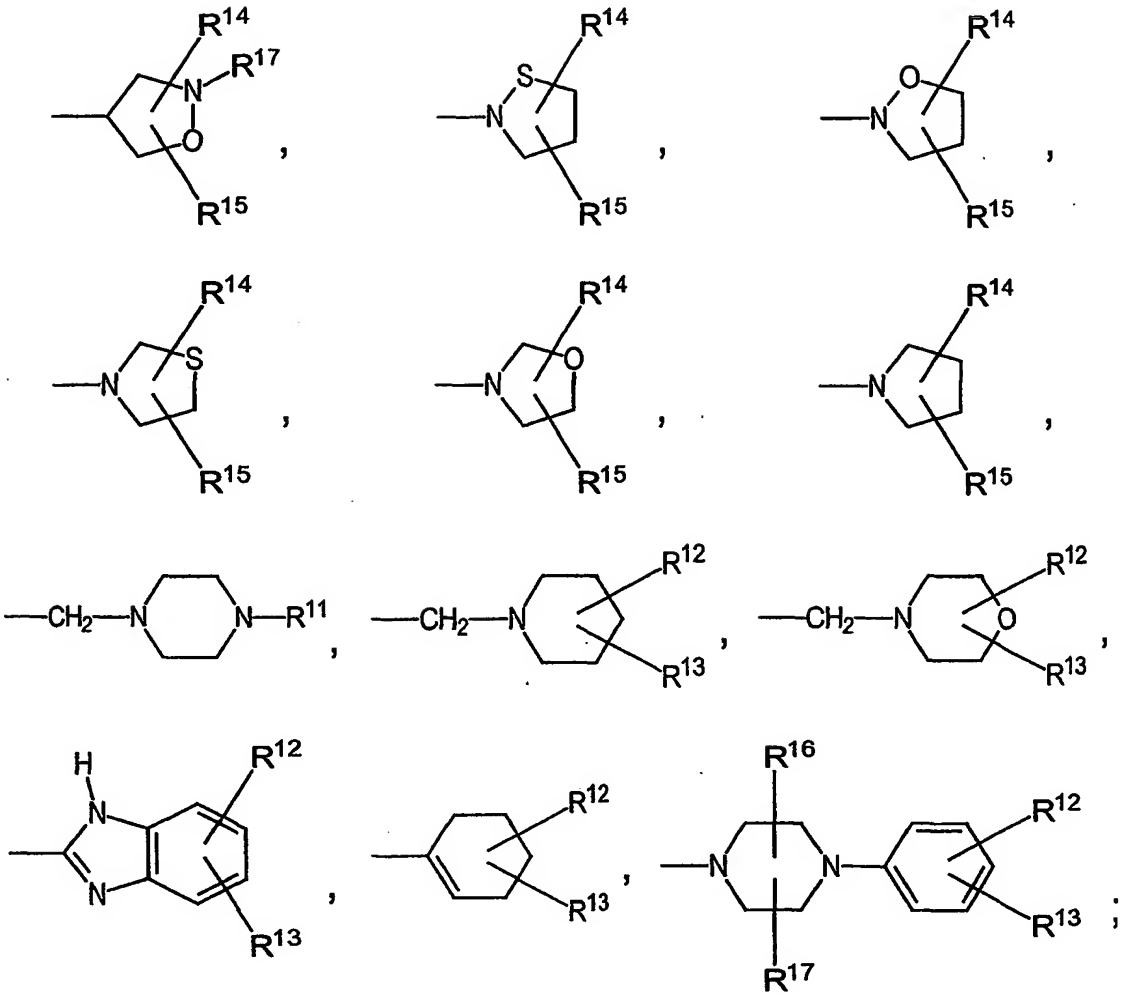
—NHR^{17},





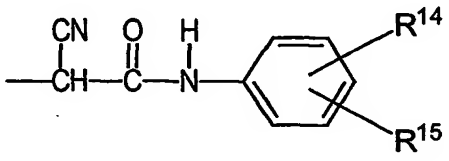




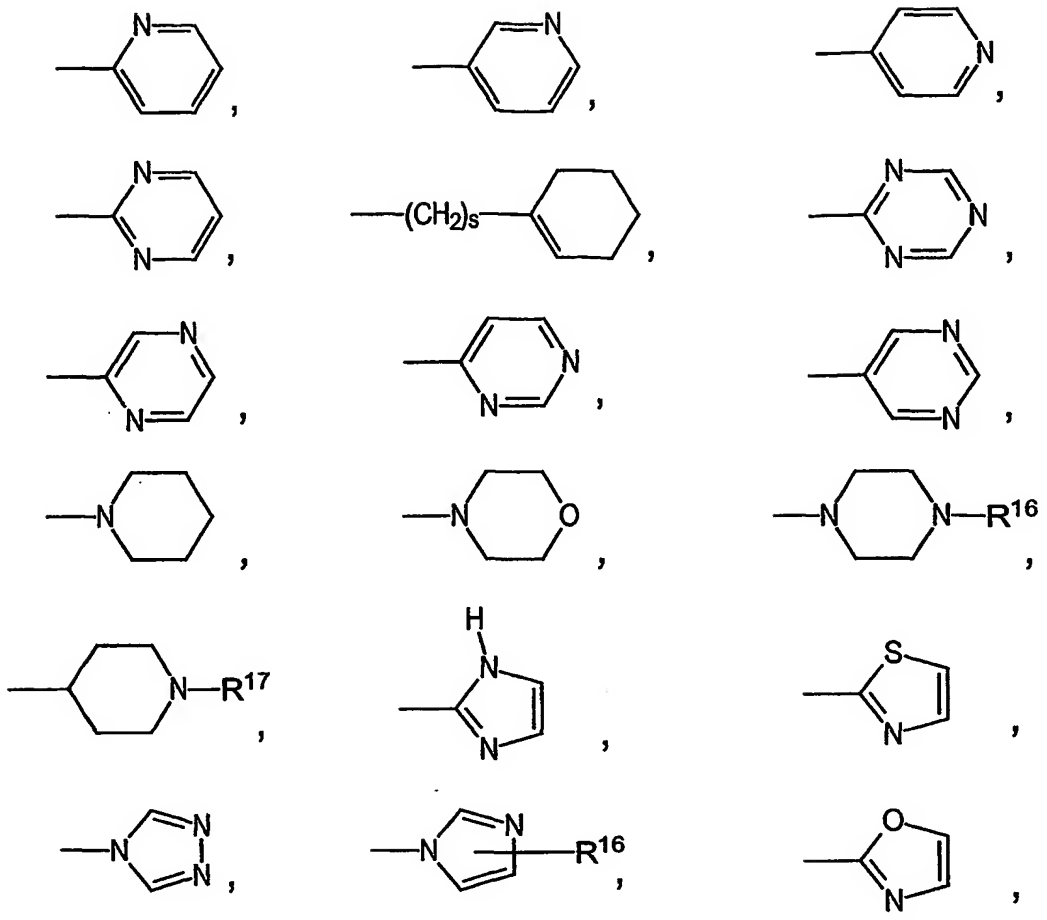
R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17},

—$CH(COOR^{16})(COOR^{17})$,

—$CH(CN)(COOR^{16})$,



R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —cyclo–C_4H_7, —cyclo–C_3H_5, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —$CH{=}CH_2$, —CH_2–$CH{=}CH_2$, —Ph, —CH_2Ph, —C_2H_4Ph, —$CH(CN)_2$, —CF_3, —CCl_3, —CBr_3, —C_2F_5, —$(CH_2)_r$–OH, —CH_2F, —CH_2Cl, —CH_2Br, —CH_2I, —CHF_2, —$CHCl_2$, —$CHBr_2$, —$(CH_2)_r$–SH, —C_6H_4–CH_3, —$C_6H_3(CH_3)_2$,



m, n, p, q, s are independently of each other integer from 0 – 6,
r is an integer from 1 – 6,
and the corresponding N-oxides in position 1 and/or 4 of these compounds;
and the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and pharmaceutically acceptable salts of these compounds.

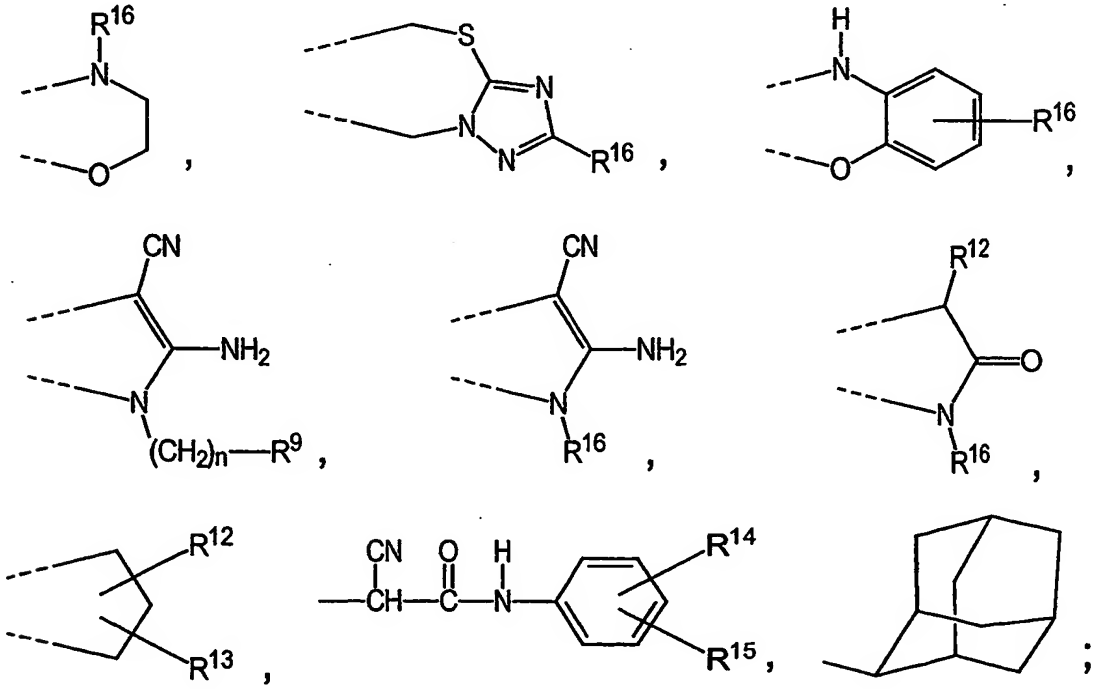
Other aspects of the present invention relate to benzo[g]quinoxaline derivatives of the general formula (I) as new pharmaceutically active agents, especially for the prophylaxis and/or treatment of mycobacteria-induced infections or diseases and mycobacteria-induced opportunistic infections, and methods for treating mycobacteria-induced infections or diseases in mammals, including humans. Such mycobacterial-induced infections or diseases comprise tuberculosis, leprosy and mycobacteria-induced meningitis.

The inventive benzo[g]quinoxaline compounds of the general formula (I) and/or pharmaceutically acceptable salts thereof are administered in a dosage corresponding to an effective concentration in the range of 0.01 – 50 µM, preferably in the range of 0.01 – 10 µM, more preferably in the range of 0.01 – 1 µM, and most preferably in the range of 0.01 – 0.1 µM.

A further aspect of the present invention relates to the use of the benzo[g]quinoxaline compounds of the general formula (I) and/or pharmaceutically acceptable salts thereof for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of mycobacteria-induced infections, including mycobacteria-induced opportunistic infections.

Preferred are these benzo[g]quinoxaline compounds wherein R^3 to R^8 represent hydrogen.

Furthermore, these benzo[g]quinoxaline derivatives are preferred wherein R^1 and R^2 are independently of each other $-(CH_2)_p-NH-(CH_2)_n-R^9$, $-(CH_2)_s-S-(CH_2)_m-R^{10}$, $-(CH_2)_m-O-(CH_2)_p-R^{11}$, $-(CH_2)_r-R^3$, $-CH=CH-R^{11}$, $-(CH_2)_m-CH(OH)-(CH_2)_p-R^{11}$, $-(CH_2)_q-R^{11}$, $-R^9$, $-R^{10}$, $-CH(COOR^{16})(COOR^{17})$, $-CH(CN)(COOR^{16})$,



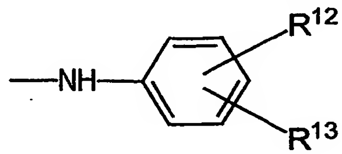
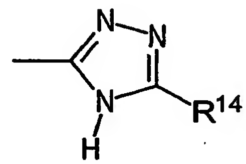
;

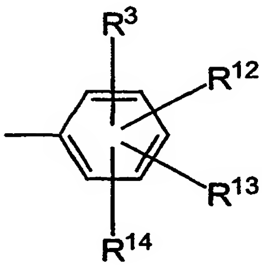
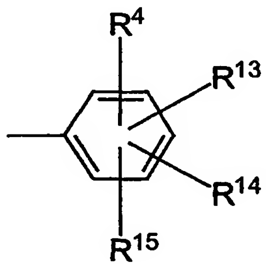
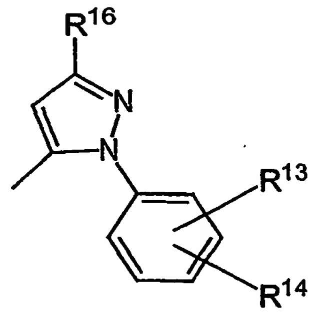
R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other —H, —F, —Cl, —Br, —I, —SO_3H, —SO_3NH_2;

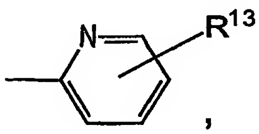
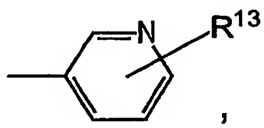
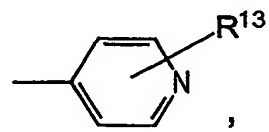
R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$,

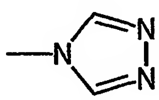
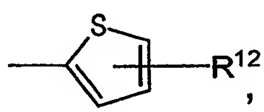
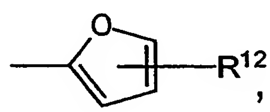
—NHR^{16},

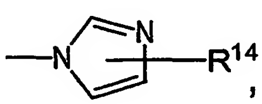
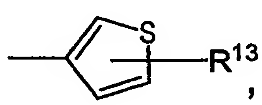
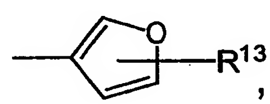
—NHR^{17},

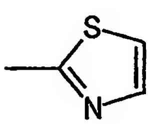
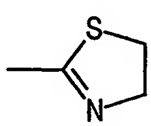
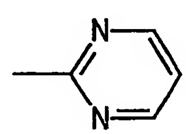
 ,
 ,

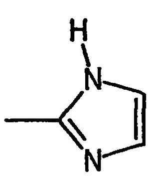
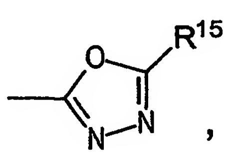
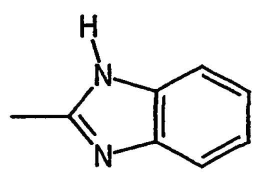
 ,
 ,
 ,

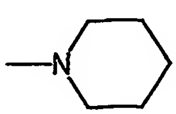
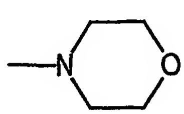
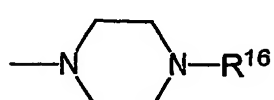
 ,
 ,
 ,

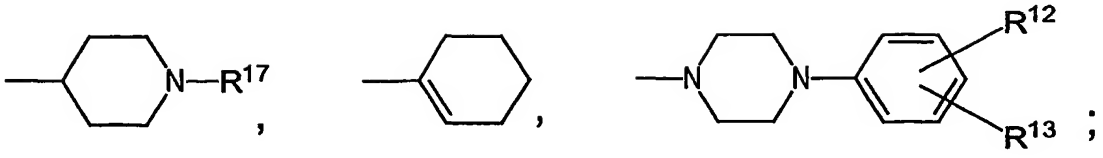
 ,
 ,
 ,

 ,
 ,
 ,

 ,
 ,
 ,

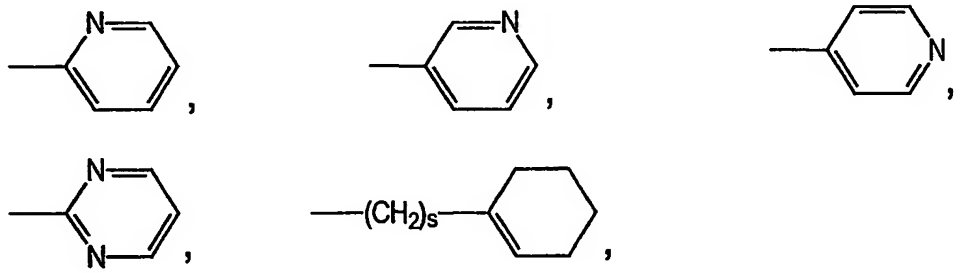
 ,
 ,
 ,

 ,
 ,
 ,



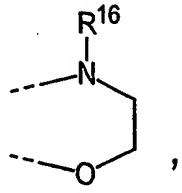
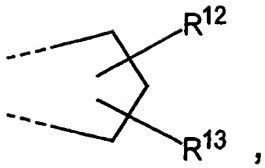
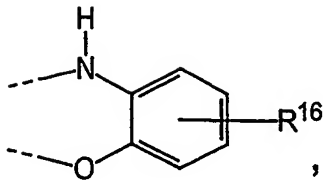
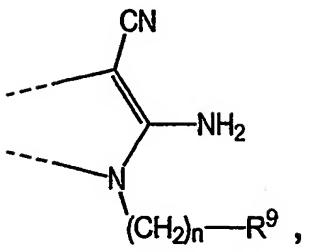
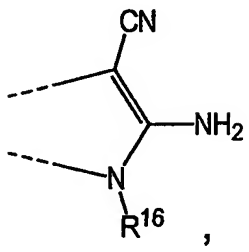
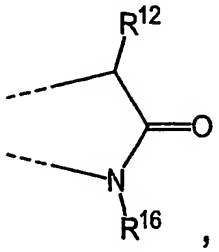
R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$(CH_2)_s$–$COOR^{16}$, —OR^{16}, —SR^{16}, —$NR^{16}R^{17}$, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};

R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —cyclo–C_4H_7, —cyclo–C_3H_5, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —$CH=CH_2$, —CH_2–$CH=CH_2$, —Ph, —CH_2Ph, —$CH(CN)_2$, —CF_3, —CCl_3, —C_2F_5, —$(CH_2)_r$–OH,



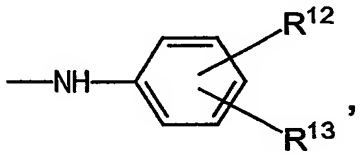
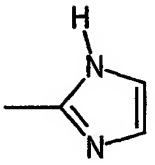
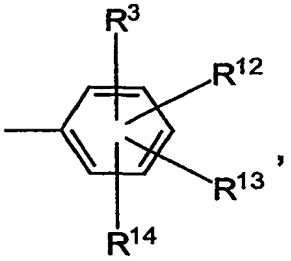
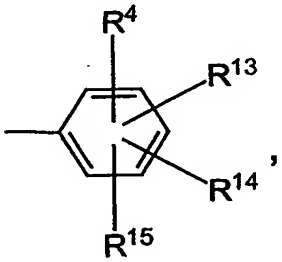
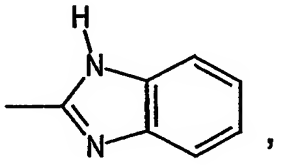
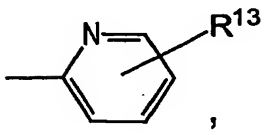
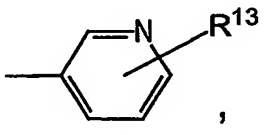
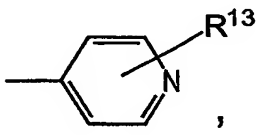
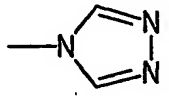
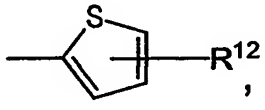
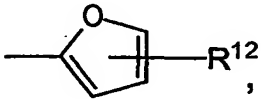
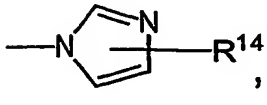
m is an integer from 0 – 6,
n is an integer from 0 – 6,
p is an integer from 0 – 6,
q is an integer from 0 – 6,
r is an integer from 1 – 6,
s is an integer from 0 – 6,
and their corresponding N-oxides in position 1 and/or 4;
and the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and pharmaceutically acceptable salts thereof.

Also preferred are these inventive benzo[g]quinoxaline compounds wherein
R^1 and R^2 are independently of each other —$(CH_2)_p$—NH—$(CH_2)_n$—R^9, —$(CH_2)_s$—S—$(CH_2)_m$—R^{10}, —$(CH_2)_r$—R^3, —CH=CH—R^{11}, —$(CH_2)_q$—R^{11}, —R^9, —R^{10}, —$CH(COOR^{16})(COOR^{17})$, —$CH(CN)(COOR^{16})$,

R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other —H, —F, —Cl, —Br, —I, —SO_3H;

R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$, —NHR^{16}, —NHR^{17},

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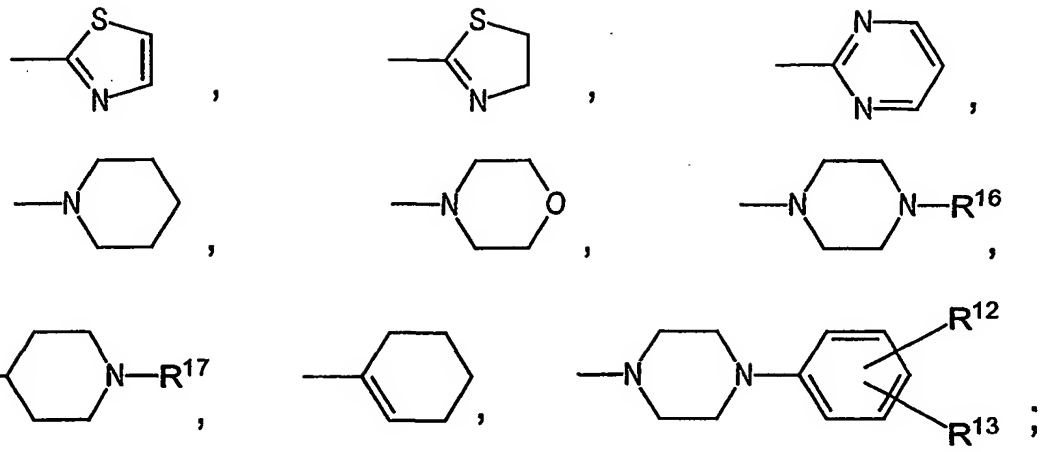
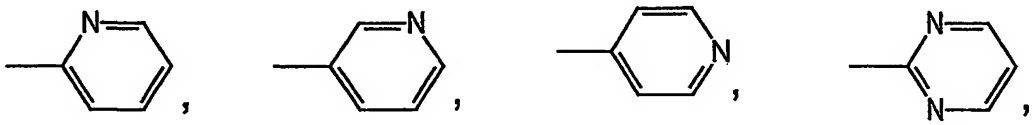


R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$(CH_2)_s$–$COOR^{16}$, —OR^{16}, —SR^{16}, —$NR^{16}R^{17}$, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};

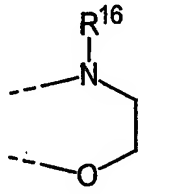
R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —CH_2–CH=CH_2, —Ph, —CH_2Ph, —$CH(CN)_2$, —CF_3, —$(CH_2)_r$–OH,



m is an integer from 0 – 6,
n is an integer from 0 – 6,
p is an integer from 0 – 6,
q is an integer from 0 – 6,
r is an integer from 1 – 6,
s is an integer from 0 – 6,
and their corresponding N-oxides in position 1 and/or 4;
and the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and pharmaceutically acceptable salts thereof.

Another group of inventive compounds comprises the following residues wherein R^1 and R^2 are independently of each other —NH—$(CH_2)_m$—R^9, —S—$(CH_2)_m$—R^{10}, —$(CH_2)_p$—NH—R^9, —$(CH_2)_s$—S—R^{10}, —CH_2—R^3,

—$(CH_2)_2$—R^3, —$(CH_2)_3$—R^3, —CH=CH—R^{11}, —CH_2—R^{11}, —$(CH_2)_2$—R^{11}, —$(CH_2)_3$—R^{11}, —CH_2—CH(OH)—R^{11}, —R^9, —R^{10}, —$CH(COOR^{16})(COOR^{17})$, —$CH(CN)(COOR^{16})$,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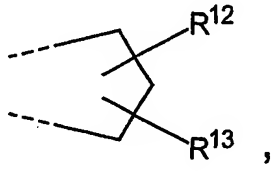
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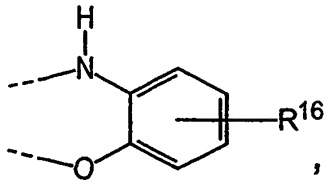
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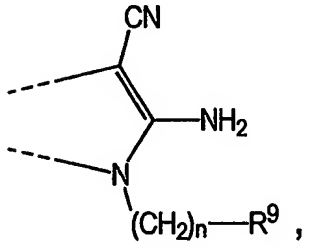
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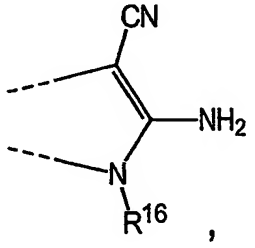
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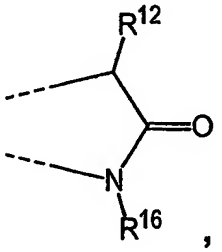
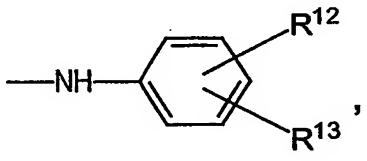

,

R^3, R^9, R^{10}, R^{11}, R^{16}, R^{17} have the meaning as defined above,
m is an integer from 0 – 4,
n is an integer from 0 – 4,
p is an integer from 0 – 4,
s is an integer from 0 – 4.

More preferred are the compounds of general formula (I) wherein
R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$, —NHR^{16}, —NHR^{17},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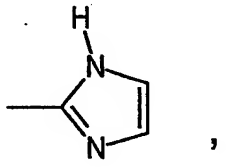
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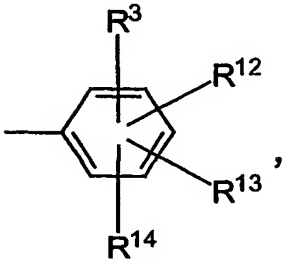
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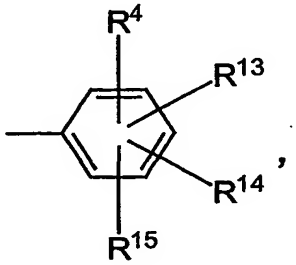
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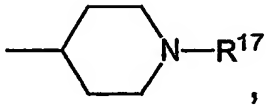
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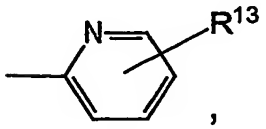
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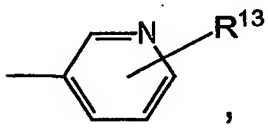
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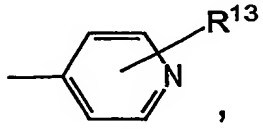
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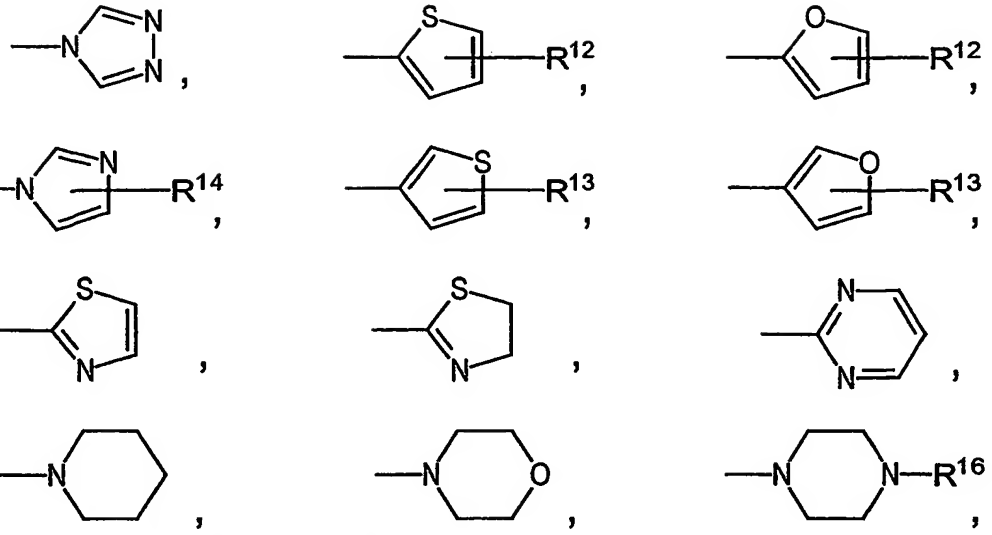
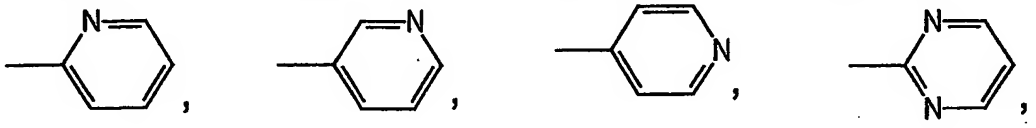


R^3, R^4, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17} have the meaning as defined above.

More preferred are also the following benzo[g]quinoxaline derivatives wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$COOR^{16}$, —CH_2–$COOR^{16}$, —$(CH_2)_2$–$COOR^{16}$, —$(CH_2)_3$–$COOR^{16}$, —OR^{16}, —SR^{16}, —NHR^{17}, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};
R^3, R^4, R^5, R^6, R^{16}, R^{17} have the meaning as defined above.

Still more preferred are the following inventive compounds wherein R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —CH_2–$CH(CH_3)_2$, —$(CH_2)_2$–$CH(CH_3)_2$, —$(CH_2)_3$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —CH_2–CH=CH_2, —Ph, —CH_2Ph, —CF_3, —$CH(CN)_2$, —CH_2–OH, —$(CH_2)_2$–OH, —$(CH_2)_3$–OH, —$(CH_2)_4$–OH,



Most preferred are the following benzo[g]quinoxaline derivatives selected from the group comprising:

(Compound 1) 1*H*-benzo[g]quinoxaline-2-one
(Compound 2) 3-Thiophen-2-yl-1*H*-benzo[g]quinoxaline-2-one
(Compound 3) 2-Chloro-benzo[g]quinoxaline
(Compound 4) 2-(2-Thienyl)-3-chloro-benzo[g]quinoxaline

(Compound 5) 2,3-Dichloro-benzo[g]quinoxaline
(Compound 6) 2,3-Thenil
(Compound 7) Bis(4,4'-methoxycarbonylmethyl)-2,2'-thenil
(Compound 8) Bis(5,5'-methoxycarbonylmethyl)-2,2'-thenil
(Compound 9) Bis(4,4'-ethoxycarbonylpropyl)-2,2'-thenil
(Compound 10) Bis(5,5'-methoxycarbonylethyl)-2,2'-thenil
(Compound 11) 1,4-Dibromo-2,3-diaminonaphthalene
(Compound 12) 2,3-Diaminonaphthalene 5-sulfonic acid sodium salt
(Compound 13) 2,3-Bis-(2-thienyl)-benzo[g]quinoxaline
(Compound 14) 2-Phenyl-benzo[g]quinoxaline
(Compound 15) 2-para-Tolylbenzo[g]quinoxaline
(Compound 16) 2-(3-Chlorophenyl)-benzo[g]quinoxaline
(Compound 17) 2-(4-Chlorophenyl)-benzo[g]quinoxaline
(Compound 18) 2-(4-Bromophenyl)-benzo[g]quinoxaline
(Compound 19) 2-Adamantan-2-yl-benzo[g]quinoxaline
(Compound 20) 2,3-Dipyridyl-2-yl-benzo[g]quinoxaline
(Compound 21) 2,3-Diphenylbenzo[g]quinoxaline
(Compound 22) 2,3-Di-para-tolyl-benzo[g]quinoxaline
(Compound 23) 2,3-Bis-(5-bromo-2-hydroxyphenyl)-benzo[g]quinoxaline
(Compound 24) 2,3-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline
(Compound 25) 2,3-Bis-(bromomethyl)-benzo[g]quinoxaline
(Compound 26) 2,3-Difuran-2-yl-benzo[g]quinoxaline
(Compound 27) 2,3-Bis-(4-fluorophenyl)-benzo[g]quinoxaline
(Compound 28) 2-Thiophen-3-yl-3-thiophen-2-yl-benzo[g]quinoxaline
(Compound 29) 2,3-Bis-(thiophen-3-yl)-benzo[g]quinoxaline
(Compound 30) 2,3-Dihydro-1H-benzo[g]cyclopenta[b]quinoxaline-1,3-dicarboxylic acid diethyl ester
(Compound 31) 2-(3,4-Dimethoxyphenyl)-benzo[g]quinoxaline
(Compound 32) 2-(3,4-Dihydroxyphenyl)-benzo[g]quinoxaline
(Compound 33) 2-Methyl-3-thiophen-2-yl-benzo[g]quinoxaline
(Compound 34) 2-Methyl-3-thiophen-2-yl-1,2-dihydro-benzo[g]-quinoxaline
(Compound 35) {5-[3-(4-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
(Compound 36) {5-[3-(5-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
(Compound 37) 2,3-Bis-(2-methoxycarbonylethyl-thiophen-5-yl)-benzo[g]-quinoxaline

(Compound 38) 2,3-Bis-(2-ethoxycarbonylpropyl-thiophen-5-yl)-benzo[g]-quinoxaline

(Compound 39) {5-[3-(4-Carboxymethyl-thiophen-2-yl)-benzo[g]-quinoxalin-2-yl]-thiophen-3-yl}-acetic acid

(Compound 40) 2,3-Bis-(2-carboxymethyl-thiophen-5-yl)-benzo[g]-quinoxaline

(Compound 41) 2,3-Bis-(2-carboxypropyl-thiophen-5-yl)-benzo[g]-quinoxaline

(Compound 42) 2,3-Bis-(2-carboxyethyl-thiophen-5-yl)-benzo[g]-quinoxaline

(Compound 43) {5-[5,10-Dibromo-3-(4-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-3-yl}-acetic acid

(Compound 44) {5-[5,10-Dibromo-3-(5-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid

(Compound 45) 2,3-Bis(4-pyridin-2-yl-piperazin-1-ylmethyl)-benzo[g]-quinoxaline hydrochloride

(Compound 46) 2,3-Bis[4-(4-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 47) 2,3-Bis[4-(2-methoxyphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 48) 2,3-Bis[4-(3-trifluoromethylphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 49) 2,3-Bis[4-(pyrimidin-2-yl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 50) 2,3-Bis[4-(3-chlorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 51) 2,3-Bis[4-(4-nitrophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 52) 2,3-Bis[4-(2-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

(Compound 53) 2,3-Bis-piperidin-1-ylmethyl-benzo[g]quinoxaline hydrochloride

(Compound 54) 2,3-Bis-morpholin-4-ylmethyl-benzo[g]quinoxaline hydrochloride

(Compound 55) 2,3-Bis-(phenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 56) 2,3-Bis-(4-methylphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 57) 2,3-Bis-(2-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 58) 2,3-Bis-(4-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 59) 2,3-Bis-(2,5-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 60) 2,3-Bis-(2,6-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 61) 2,3-Bis-(3,4-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 62) 2,3-Bis-(2,4-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 63) 2,3-Bis-(2,5-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 64) 2,3-Bis-(2,3,5,6-tetrafluorophenylsulfanylmethyl)-benzo[g]-quinoxaline

(Compound 65) 2,3-Bis-(2-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 66) 2,3-Bis-(3-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 67) 2,3-Bis-(4-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 68) 2,3-Bis-(2-bromophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 69) 2,3-Bis-(3-bromophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 70) 2,3-Bis-(4-fluorophenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 71) 2,3-Bis-(2-methylphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 72) 2,3-Bis-(3-methylphenylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 73) 2,3-Bis-(4,5-dihydro-thiazol-2-yl-sulfanylmethyl)-benzo[g]-quinoxaline

(Compound 74) 2,3-Bis-(1H-benzoimidazol-2-ylsulfanylmethyl)-benzo[g]quinoxaline

(Compound 75) (3-Methoxycarbonylmethylsulfanylmethyl-benzo[g]-quinoxalin-2-ylmethylsulfanyl)-acetic acid methyl ester

(Compound 76) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malononitrile

(Compound 77) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malonic acid diethyl ester

(Compound 78) (3-Chloro-benzo[g]quinoxalin-2-yl)-cyano-acetic acid ethyl ester

(Compound 79) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-2-cyano-N-(4-trifluoromethyl-phenyl)-acetamide

(Compound 80) N-(3,5-Bis-trifluoromethyl-phenyl)-2-(3-chloro-benzo[g]quinoxalin-2-yl)-2-cyano-acetamide

(Compound 81) Benzo[g]quinoxalin-2-yl-(2-ethoxycarbonylphenyl)-amine

(Compound 82) 4-(Benzo[g]quinoxalin-2-ylamino)-benzenesulfonamide

(Compound 83) Benzo[g]quinoxalin-2-yl-(3,4-dimethylphenyl)-amine

(Compound 84) Benzo[g]quinoxalin-2-yl-[3,5-bis-(ethoxycarbonyl)-phenyl] amine

(Compound 85) Benzo[g]quinoxalin-2-yl-(2-hydroxy-4-methylphenyl)-amine
(Compound 86) Benzo[g]quinoxaline-2-yl-phenylamine
(Compound 87) Benzo[g]quinoxalin-2-yl-biphenyl-4-yl-amine
(Compound 88) Benzo[g]quinoxalin-2-yl-(4-methylphenyl)-amine
(Compound 89) Benzo[g]quinoxalin-2-yl-(4-phenoxyphenyl)-amine
(Compound 90) Benzo[g]quinoxalin-2-yl-(4-bromophenyl)-amine
(Compound 91) Benzo[g]quinoxalin-2-yl-(4-methylsulfanylphenyl)-amine
(Compound 92) [4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-phenylmethanone
(Compound 93) Benzo[g]quinoxalin-2-yl-(2,4-dimethoxyphenyl)-amine
(Compound 94) Benzo[g]quinoxalin-2-yl-(2-hydroxy-5-chlorophenyl)-amine
(Compound 95) Benzo[g]quinoxalin-2-yl-(3-fluoro-4-methylphenyl)-amine
(Compound 96) Benzo[g]quinoxalin-2-yl-[2-(2-chlorophenyl)-ethyl]-amine
(Compound 97) Benzo[g]quinoxalin-2-yl-(3-bromophenyl)-amine
(Compound 98) Benzo[g]quinoxaline-2-yl-(3,4-dimethoxyphenyl)-amine
(Compound 99) 4-(Benzo[g]quinoxaline-2-yl-amino)-benzene-1,2-diol
(Compound 100) N-Benzo[g]quinoxalin-2-yl-N'-(4-fluorophenyl)-hydrazine
(Compound 101) N-Benzo[g]quinoxalin-2-yl-N'-(2,4-dichlorophenyl)-hydrazine
(Compound 102) N-Benzo[g]quinoxalin-2-yl-N'-(3-chlorophenyl)-hydrazine
(Compound 103) N-Benzo[g]quinoxalin-2-yl-N'-(4-chlorophenyl)-hydrazine
(Compound 104) 1-(2-Nitrophenyl)-2-(3-thiophen-2-yl-benzo[g]quinoxaline-2-yl)-ethanol
(Compound 105) Benzo[g]quinoxalin-2-yl-(4-ethylphenyl)-amine
(Compound 106) N-[4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide
(Compound 107) Benzo[g]quinoxalin-2-yl-(3-chlorophenyl)-amine
(Compound 108) Benzo[g]quinoxalin-2-yl-(4-chlorophenyl)-amine
(Compound 109) Benzo[g]quinoxalin-2-yl-(3-fluorophenyl)-amine
(Compound 110) Benzo[g]quinoxalin-2-yl-(2-fluorophenyl)-amine
(Compound 111) Benzo[g]quinoxalin-2-yl-(2,4-dichlorophenyl)-amine
(Compound 112) Benzo[g]quinoxalin-2-yl-(4-hydroxyphenyl)-amine
(Compound 113) Benzo[g]quinoxalin-2-yl-(3-iodophenyl)-amine
(Compound 114) Benzo[g]quinoxalin-2-yl-(3,4-dichlorophenyl)-amine
(Compound 115) Benzo[g]quinoxalin-2-yl-(3-trifluoromethylphenyl)-amine
(Compound 116) Benzo[g]quinoxalin-2-yl-(4-trifluoromethylphenyl)-amine
(Compound 117) (5-Chloro-2-methylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine
(Compound 118) (2-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 119) (4-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine

(Compound 120) (3,4-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 121) (2,5-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 122) (4-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 123) (3-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 124) (3-Hydroxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 125) N-[4-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide

(Compound 126) (2-Hydroxy-4-methylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 127) (3-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 128) (4-Bromophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 129) (3-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 130) (2-Morpholin-4-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 131) [3-(4-Methylpiperazin-1-yl)-propyl]-(3-thiophen-2-yl-benzo[g]-quinoxalin-2-yl)-amine

(Compound 132) (2-Piperidin-1-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 133) N-(3-Bromophenyl)-N'-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-hydrazine

(Compound 134) (4-Butylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

(Compound 135) Benzo[g]quinoxalin-2-yl-[2-(2-bromo-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

(Compound 136) Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(3-nitro-phenyl)-2H-pyrazol-3-yl]-amine

(Compound 137) Benzo[g]quinoxalin-2-yl-[2-(3-fluoro-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

(Compound 138) Benzo[g]quinoxalin-2-yl-[2-(3-trifluoromethyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

(Compound 139) Benzo[g]quinoxalin-2-yl-[2-(2-methyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

(Compound 140) Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(4-nitro-phenyl)-2H-pyrazol-3-yl]-amine

(Compound 141) [5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-(3-chloro-benzo[g]-quinoxalin-2-yl)-amine

(Compound 142) [5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

(Compound 143) [5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

(Compound 144) [5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

(Compound 145) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 146) 2-(3-([5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

(Compound 147) 2-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

(Compound 148) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 149) 3-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol

(Compound 150) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 151) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 152) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 153) 3-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino])-benzo[g]quinoxalin-2-yl-amino)-propanol

(Compound 154) 3-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol

(Compound 155) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 156) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 157) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 158) 2-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-ethanol

(Compound 159) N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 160) N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 161) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 162) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 163) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine

(Compound 164) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 165) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 166) 2-[(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-amino)-benzo[g]quinoxalin-2-yl)-(2-hydroxyethyl)-amino]-ethanol

(Compound 167) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-4-yl-methyl-benzo[g]quinoxaline-2,3-diamine

(Compound 168) N-(1-Benzylpiperidin-4-yl-methyl)-N'-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-benzo[g]quinoxaline-2,3-diamine

(Compound 169) 2-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

(Compound 170) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 171) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 172) N,N'-Dipyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine

(Compound 173) N,N'-Diphenyl-benzo[g]quinoxaline-2,3-diamine

(Compound 174) N,N'-Bis-[1,2,4]triazol-4-yl-benzo[g]quinoxaline-2,3-diamine

(Compound 175) N,N'-Bis-(4-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 176) N,N'-Bis-(4-bromophenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 177) N,N'-Bis-(4-phenoxyphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 178) N,N'-Bis-(3,4-dimethyl-phenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 179) N,N'-Bis-(4-methylsulfanylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 180) N,N'-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 181) N,N'-Bis-(3-chloro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 182) N,N'-Bis-(3-bromophenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 183) N,N'-Bis-(3-fluorophenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 184) N,N'-Bis-(3-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 185) N,N'-Bis-(3-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 186) N,N'-Bis-(4-ethylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 187) N,N'-Bis-(4-butylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 188) N,N'-Bis-(3-trifluoromethylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 189) N,N'-Bis-(3,4-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 190) N,N'-Bis-(3-fluoro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 191) N,N'-Bis-(4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 192) N,N'-Bis-(2,5-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine.

(Compound 193) N-{4-[3-(4-Acetylaminophenylamino)-benzo[g]quinoxalin-2-yl-amino]-phenyl}-acetamide

(Compound 194) N,N'-Bis-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 195) N,N'-Bis-(2-hydroxyethyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 196) N,N'-Bis-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 197) N,N'-Bis-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 198) N,N'-Bis-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 199) N,N'-Dipyridin-4-yl-benzo[g]quinoxaline-2,3-diamine

(Compound 200) N,N'-Bis-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 201) N,N'-Bis-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

(Compound 202) N,N'-Bis-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 203) N,N'-Bis-(1-benzylpiperidin-4-yl)-benzo[g]quinoxaline-2,3-diamine

(Compound 204) N,N'-Bis-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 205) N,N'-Bis-(3-hydroxypropyl)-benzo[g]quinoxaline-2,3-diamine

(Compound 206) 2-Piperidin-1-yl-benzo[g]quinoxaline

(Compound 207) 1-Benzo[g]quinoxalin-2-yl-piperidine-4-carboxylic acid ethyl ester

(Compound 208) 2-Morpholin-4-yl-benzo[g]quinoxaline

(Compound 209) 2-(4-Methyl-piperazin-1-yl)-benzo[g]quinoxaline

(Compound 210) 4-Benzo[g]quinoxalin-2-yl-piperazine-1-carboxylic acid ethyl ester

(Compound 211) 2-(4-Phenyl-piperazin-1-yl)-benzo[g]quinoxaline

(Compound 212) 2-Morpholin-4-yl-3-thiophen-2-yl-benzo[g]quinoxaline

(Compound 213) 1-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl)-piperidine-4-carboxylic acid ethyl ester

(Compound 214) 2-[4-(4-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline

(Compound 215) 2-[4-(3-Trifluoromethyl-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline

(Compound 216) 2-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline

(Compound 217) 2-(4-Pyridin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline

(Compound 218) 2-(4-Pyrimidin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline

(Compound 219) 2-[4-(2-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline

(Compound 220) (3-Chloro-benzo[g]quinoxalin-2-yl)-(4-chlorophenyl)-amine

(Compound 221) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-4-fluoro-phenyl)-amine

(Compound 222) (4-Bromo-phenyl)-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

(Compound 223) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-fluoro-phenyl)-amine

(Compound 224) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-phenyl)-amine

(Compound 225) (3-Chloro-benzo[g]quinoxalin-2-yl)-(4-trifluoromethyl-phenyl)-amine

(Compound 226) 2-(4-Chloro-phenoxy)-benzo[g]quinoxaline

(Compound 227) 2-(4-Bromo-phenoxy)-benzo[g]quinoxaline

(Compound 228) 2-(3-Methoxy-phenoxy)-benzo[g]quinoxaline

(Compound 229) 2-(4-Methoxy-phenoxy)-benzo[g]quinoxaline

(Compound 230) 2-(3,5-Dimethoxy-phenoxy)-benzo[g]quinoxaline

(Compound 231) 2-(4-Bromo-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

(Compound 232) 2-(4-Chloro-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

(Compound 233) 2-(3,5-Dimethoxy-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

(Compound 234) 2-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 235) 2-(1H-Imidazol-2-yl-sulfanyl)-benzo[g]quinoxaline

(Compound 236) 2-(1H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]-quinoxaline

(Compound 237) 2-(Pyrimidin-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]quinoxaline

(Compound 238) 2-(1H-Imidazol-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline

(Compound 239) 2-(2,5-Dichloro-phenylsulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline

(Compound 240) 2-(Pyrimidin-2-yl-sulfanyl)-benzo[g]quinoxaline

(Compound 241) 4-(3-Chloro-benzo[g]quinoxalin-2-ylsulfanyl)-phenylamine

(Compound 242) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 243) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 244) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 245)(3-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 246) [3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-chloro-phenyl)-amine

(Compound 247)(3-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 248) (3-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 249) (3-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 250) (3-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 251) (3-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 252) (3-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 253) (3-Chloro-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 254) (3-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 255) (3-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

(Compound 256) [3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 257) [3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 258) [3-(2,4-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 259) [3-(2-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 260) [3-(2-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 261) [3-(3-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 262) [3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 263) [3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 264) [3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 265) [3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 266) [3-(3-p-Tolylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 267) [3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

(Compound 268) [3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-trifluoromethyl-phenyl)-amine

(Compound 269) [3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 270) [3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 271) [3-(2,4-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 272) [3-(2-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 273) [3-(2-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 274) [3-(3-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 275) [3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 276) [3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 277) [3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 278) [3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 279) (3-Fluorophenyl)-(3-p-toylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

(Compound 280) [3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 281) [3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 282) [3-(2,6-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

(Compound 283)(4-Bromo-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 284) (4-Bromo-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 285) (4-Bromo-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 286) (4-Bromo-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 287) (4-Bromo-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 288) (4-Bromo-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 289) (4-Bromo-phenyl)-(3-phenylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

(Compound 290) (4-Bromo-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 291) (4-Bromo-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 292) (4-Bromo-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 293) (4-Bromo-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

(Compound 294) (4-Bromo-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 295) (4-Bromo-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 296) (4-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 297) (4-Chloro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 298) (4-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 299) (4-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 300) (4-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 301) (4-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 302) (4-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 303) (4-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 304) (4-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 305) (4-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

(Compound 306) (4-Chloro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 307) (3-Chloro-4-fluoro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 308) (3-Chloro-4-fluoro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 309) (3-Chloro-4-fluoro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 310) (3-Chloro-4-fluoro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 311) (3-Chloro-4-fluoro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 312) (3-Chloro-4-fluoro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 313) (3-Chloro-4-fluoro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 314) (3-Chloro-4-fluoro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 315) (3-Chloro-4-fluoro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 316) (3-Chloro-4-fluoro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl]-amine

(Compound 317) (3-Chloro-4-fluoro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 318) (3-Chloro-4-fluoro-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

(Compound 319) 2,3-Bis-(3-chloro-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 320) 2,3-Bis-(naphthalen-2-yl-sulfanyl)-benzo[g]quinoxaline

(Compound 321) 2,3-Bis-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 322) 2,3-Bis-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 323) 2,3-Bis-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 324) 2,3-Bis-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 325) 2,3-Bis-(3-bromo-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 326) 2,3-Bis-(4-methyl-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 327) 2,3-Bis-(3-methyl-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 328) 2,3-Bis-(5-amino-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]-quinoxaline

(Compound 329) 2,3-Bis--(5-pyridin-4-yl-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]-quinoxaline

(Compound 330) 2,3-Bis-(5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]-quinoxaline

(Compound 331) 2,3-Bis-(2-methyl-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 332) 2,3-Bis-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 333) 2,3-Bis-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 334) 2,3-Bis-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 335) 2,3-Bis-(4-amino-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 336) 2,3-Bis-(3-amino-phenylsulfanyl)-benzo[g]quinoxaline

(Compound 337) 2,3-Bis-(1H-imidazol-2-ylsulfanyl)-benzo[g]quinoxaline

(Compound 338) 4-[3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 339) 4-[3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 340) 4-[3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 341) 4-[3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 342) 4-[3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 343) 4-[3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

(Compound 344) 2-Pyridin-4-yl-4,13-dihydro-14-thia-1,3,3a,5,12-pentaaza-azuleno[5,6-b]anthracene

(Compound 345) Benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 346) 3-(3,4-Dimethoxy-.phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 347) 2-Methyl-3-phenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 348) 2,3-Diphenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 349) 2,3-Di-p-tolyl -benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 350) 2,3-Di-furan-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 351) 2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 352) 2,3-Dithiophenyl-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

(Compound 353) 2,3-Diphenyl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

(Compound 354) 3-(3,5-Bis-trifluoromethyl-phenyl)-benzo[g]quinoxaline-7-sulfonic acid sodium salt

(Compound 355) 2,3-Di-thiophen-3-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

(Compound 356) 2,3-Di-pyridin-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

(Compound 357) 2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

(Compound 358) 2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-7-sulfon amide

(Compound 359) 2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-6-sulfonamide

(Compound 360) 2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline-6-sulfonamide

(Compound 361) 5,10-Dibromo-2-(3-chloro-phenyl)-benzo[g]quinoxaline
(Compound 362) 2-(3,5-Bis-trifluoromethyl-phenyl)-5,10-dibromo-benzo[g]-quinoxaline
(Compound 363) 5,10-Dibromo-2-(3,4-dimethoxy-phenyl)-benzo[g]quinoxaline
(Compound 364) 5,10-Dibromo-2-methyl-3-phenyl)-benzo[g]-quinoxaline
(Compound 365) 5,10-Dibromo-2,3-di-thiophen-2-yl-benzo[g]quinoxaline
(Compound 366) 5,10-Dibromo-2-thiophen-3-yl-3-thiophen-2-yl-benzo [g] – quinoxaline
(Compound 367) 5,10-Dibromo-2,3-di-thiophen-3-yl-benzo[g]quinoxaline
(Compound 368) 5,10-Dibromo-2,3-bis-(5-bromo-2-hydroxy-phenyl)-benzo[g]quinoxaline
(Compound 369) 5,10-Dibromo-2,3-di-furan-2-yl-benzo[g]quinoxaline
(Compound 370) 5,10-Dibromo-2,3-di-pyridin-2-yl- benzo[g]quinoxaline
(Compound 371) 5,10-Dibromo-2,3-bis-(3-methoxy-phenyl)-benzo[g]quinoxaline
(Compound 372) 5,10-Dibromo-2,3-bis -phenyl-benzo[g]quinoxaline
(Compound 373) 5,10-Dibromo-2,3-bis-(4-methyl-phenyl)-benzo[g]quinoxaline
(Compound 374) 5,10-Dibromo-2,3-bis-(4-bromo-phenyl)-benzo[g]quinoxaline
(Compound 375) 5,10-Dibromo-2,3-bis-(4-fluoro-phenyl)-benzo[g]quinoxaline
(Compound 376) 5,10-Dibromo-2,3-bis-(4-methoxy-phenyl)-benzo[g]quinoxaline
(Compound 377) {5-[5,10-Dibromo-3-(5-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
(Compound 378) {5-[5,10-dibromo-3-(4-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
(Compound 379) 2,3-Di-thiophen-2-yl-1,2,3,4-tetrahydro-benzo[g]quinoxaline
(Compound 380) 3-(5-{3-[5-(2-Carboxy-ethyl)-thiophen-2-yl]-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl}-thiophen-2-yl)-propionic acid
(Compound 381) 3-Thiophen-2-yl-3,4-dihydro-1H-benzo[g]quinoxalin-2-one
(Compound 382) {5-[3-(5-Carboxymethyl-thiophen-2-yl)-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid
(Compound 383) 3,4-Dihydro-1H-benzo[g]quinoxalin-2-one
(Compound 384) 2-(3,5-bis-(trifluoromethyl)-phenyl)-benzo[g]quinoxaline-N-oxide
(Compound 385) 2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline 1,4-dioxide
(Compound 386) 2-Amino-1-(2-thiophen-2-yl-ethyl)-1H-benzo[g]pyrrolo[2,3-b] quinoxaline-3-carbonitrile
(Compound 387) 2-Amino-1-(2-hydroxy-ethyl)-1H-benzo[g]pyrrolo-[2,3-b] - quinoxaline-3-carbonitrile

(Compound 388) 2-Amino-1-(3-methyl-butyl)-1H-benzo[g]pyrrolo-[2,3-b] - quinoxaline-3-carbonitrile

(Compound 389) 2-Amino-1-(2-hydroxy-propyl)-1H-benzo[g]pyrrolo-[2,3-b] - quinoxaline-3-carbonitrile

(Compound 390) 2-Amino-1-[2-(3-fluoro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile

(Compound 391) 2-Amino-1-[2-(3-chloro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile

(Compound 392) 2-Amino-1-[2-(4-methoxy-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile

(Compound 393) 2-Amino-1-(2-cyclohex-1-enyl-ethyl)-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile

(Compound 394) 2-Amino-1-(3-imidazol-1-yl-propyl)-1H-benzo[g]pyrrolo-[2,3-b] -quinoxaline-3-carbonitrile

(Compound 395) 1-(2-Hydroxy-ethyl)-2-oxo-2,3-dihydro-1H-benzo[g]pyrrolo[2,3-b]quinoxaline-3-carboxylic acid ethyl ester

(Compound 396) 2-(2,3-Dihydro-1-oxa-4,5,12-triaza-naphthacen-4-yl)-ethanol

(Compound 397) 2-[2-(2,4-Dichlorophenyl)-vinyl]-3-thiophen-2-yl-benzo[g]-quinoxaline

(Compound 398) 1,2,3,4-Tetrahydrobenzo[b]phenazine

(Compound 399) 2-(5-Pyridin-4-yl-1H-[1,2,4]triazole-3-ylsulfanyl)-benzo[g]quinoxaline

(Compound 400) 2-(1H-Benzoimidazole-2-ylsulfanyl)-benzo[g]quinoxaline

(Compound 401) 2-(4-Nitrophenyl)-benzo[g]quinoxaline

(Compound 402) 2,3-Dimethyl-benzo[g]quinoxaline

(Compound 403) 2-Phenyl-3-trifluoromethyl-benzo[g]quinoxaline

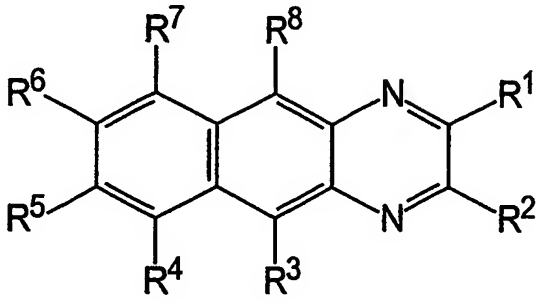
(Compound 404) 2-Methyl-3-phenyl-benzo[g]quinoxaline

(Compound 405) 2,3-Bis-(4-bromophenyl)-benzo[g]quinoxaline

(Compound 406) 2-(4-Fluorophenyl)-benzo[g]quinoxaline

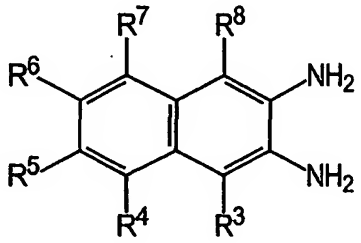
and/or pharmaceutically acceptable salts thereof.

The inventive benzo[g]-quinoxaline compounds of the general formula (I)



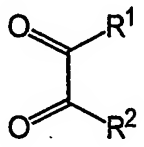
wherein the substituents $R^1 - R^8$ have the meanings as defined above and/or salts of these compounds can be synthesized according to the following procedures.

A 2,3-diaminonaphthalene compound of the general formula (II)



(II)

is dissolved in a polar solvent, preferably DMF, N,N-dimethylacetamide, acetic acid, methanol, ethanol, propanol, isopropanol, THF, dioxane, acetone or mixtures of these solvents and is treated with a 1,2-diketone of the general formula (III)



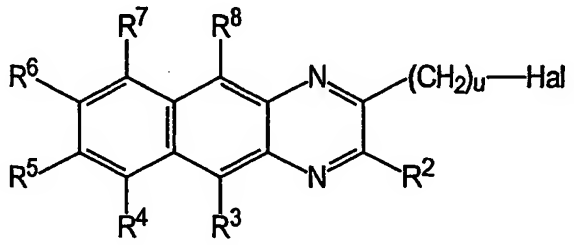
(III)

which may also be dissolved in one of the polar solvents as mentioned above. The reaction is carried out at elevated reaction temperatures, preferably at the boiling point of the solvent or solvent mixture for a time period ranging from 30 minutes to 24h, depending on the reactants, solvents, and reaction temperature. Preferred are reaction temperatures of 50 – 160°C, more preferably 60 – 120°C, still more preferably 70 – 100°C, and most preferably 75 – 85°C. Reaction times

are preferably between 0.5 – 10h, more preferably between 1 – 5h, and most preferably between 2 and 4 hours.

Under normal conditions the product precipitates during the reaction and can be isolated by filtration. Preferably, the product is washed with ether and dried in vacuum. Further purification can be obtained by recrystallization or column chromatography or any other method known to a person skilled in the art.

An alternative process for the synthesis of the benzo[g]-quinoxaline compounds of the present invention starts with a halogen-benzo[g]quinoxaline compound of the general formula (IV)



(IV)

wherein R^2 – R^8 have the meanings as defined above and wherein Hal represents a halogen selected from —F, —Cl, —Br, —I, preferably —Cl or —Br. The integer u can be selected from 0 – 6, preferably 0 or 1. This compound is dissolved in a preferably anhydrous aprotic medium such as dioxane or THF when an activated methylene compound is used as nucleophile or in a polar protic or aprotic solvent such as DMF, N,N-dimethylacetamide, methanol, ethanol, propanol, THF, dioxane, acetone or mixtures thereof in the case a amine, thiol, or alcohol is used as nucleophile.

The nucleophile has the general formula (V)

$$H—R^{1'} \qquad (V)$$

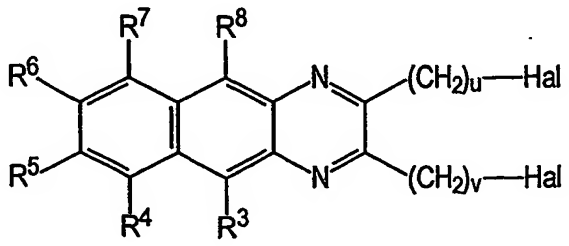
and the substituent $—(CH_2)_u—R^{1'}$ has the meaning of R^1 as defined above. The reactant (V) may optionally be dissolved in a suitable polar solvent. Depending on the nucleophile, the use of a base such as NaH, BuLi, MeLi, tert.-BuLi, K-t-BuO, K_2CO_3, triethylamine, pyridine, sodium acetate, sodium benzoate and preferably NaH is necessary. Said nucleophiles which require the addition of a base are

activated methylene compounds, alcohols, and thiols. If amines are used as nucleophiles, a tertiary amine such as triethylamine or pyridine may optionally added to the reaction mixture before the addition of the nucleophile. Thiols as nucleophile require only weak bases such as acetates or benzoates, while alcohols are preferably reacted with the compound of general formula (IV) by means of carbonates or alkoxides. Strong bases such as NaH, BuLi, MeLi, or tert.-BuLi are used for methylene compounds.

The reaction is carried out preferably under elevated temperatures and more preferably at the boiling point of the solvent or solvent mixture refluxing the reaction mixture for a time period ranging from 30 minutes to 24h depending on the reactants, solvents and reaction temperature. Preferred are reaction temperatures of 20 – 100°C, more preferably 25 – 70°C, and most preferably 30 – 60°C. Reaction times are preferably between 0.5 – 24h, more preferably between 1 – 10h, and most preferably between 2 and 4 hours. An increase of the reaction temperature will decrease the reaction time. Thus, reactions carried out at about 50°C need normally to be refluxed for not more than 4 hours. The addition of a strong base does normally not require an elevated reaction temperature in order to complete the reaction within 0.5 to 4 hours. Similar conditions can also be applied to the third alternative process mentioned below.

Under normal conditions the product precipitates during the reaction and can be isolated by filtration. Preferably, the product is washed with ether and dried in vacuum. Further purification can be obtained by recrystallization or column chromatography or any other method known to a person skilled in the art.

A third alternative process for manufacturing the inventive benzo[g]-quinoxaline compounds uses the following dihalo compound of the general formula (VI)



(VI)

wherein Hal represents a halogen selected from —F, —Cl, —Br, —I, and u and v are independently of each other an integer from 0 – 6.

Said dihalo compound is reacted either with at least two mol equivalents of a nucleophile of the general formula

$$H—R^{1'} \qquad (V)$$

wherein the substituent $—(CH_2)_u—R^{1'}$ has the meaning of R^1 as defined above, or in a first step with approximately one mol equivalent of a nucleophile having the general formula

$$H—R^{1'} \qquad (V)$$

and in a second reaction step with another nucleophile of the general formula (VII)

$$H—R^{2'} \qquad (VII)$$

in a polar solvent optionally at elevated reaction temperatures. The substituent $—(CH_2)_v—R^{2'}$ has the meaning of R^2 as defined above. Reaction conditions, solvents, nucleophiles, and the use of an additional base are comparable with these used for the monohalo compound as described previously.

Normally amines react faster than thiols and these reactions can be carried out at room temperature or slightly elevated temperatures up to 60°C while thiols normally need to be refluxed, preferably at temperatures between 70 and 100°C.

The present invention relates to a method for down-regulating or inhibiting growth and/or inducing death of *Mycobacterium tuberculosis* in an individual comprising the step of administering a pharmaceutically effective amount of an inventive benzo[g]quinoxaline compound.

A further aspect is directed to a method for preventing and/or treating *Mycobacterium tuberculosis* induced infections and diseases, including *Mycobacterium tuberculosis* induced opportunistic infections in an individual or in cells comprising the step of administering a pharmaceutically effective amount of a benzo[g]quinoxaline derivative.

It is supposed that mycobacterial protein kinases are possible targets for the pharmaceutically active benzo[g]quinoxaline derivatives of the present invention. Particularly, the present invention provides benzo[g]quinoxaline derivatives as effective compounds against mycobacterial infections and diseases, including mycobacterial-induced opportunistic infections, and a method for prophylaxis and/or treatment of infectious diseases caused by mycobacteria. Especially, the inventive compounds are able to at least partially inhibit serine-threonine protein kinases of *Mycobacterium tuberculosis*, for instance Pkn A, Pkn B, Pkn D, Pkn E, Pkn F, Pkn G, Pkn H, Pkn I, Pkn J, Pkn K and Pkn L.

Surprisingly, it was found that the benzo[g]quinoxaline derivatives of the general formula (I) are effective compounds for prophylaxis and/or treatment of mycobacteria-induced infections and diseases, including mycobacteria-induced opportunistic infections. Especially these mycobacteria-induced infections and diseases are tuberculosis, leprosy or mycobacteria-induced meningitis. Mycobacteria which induce or cause these infections and diseases, including opportunistic infections, are members of the group comprising the tuberculous mycobacteria *M. tuberculosis, M. bovis,* and *M. africanum,* the mycobacterium *M. leprae* and the nontuberculous mycobacteria *M. abscessus, M. avium, M. celatum, M. chelonae, M. fortuitum, M. genavense, M. gordonae, M. haemophilum, M. intracellulare, M. kansaii, M. malmoense, M. marinum, M. scrofulaceum, M. simiae, M. szulgai, M. ulcerans* and *M. xenopi.* Because of the overwhelming clinical importance of tuberculosis, mycobacteriologists have distinguished the *Mycobacterium tuberculosis* complex, consisting of *M. tuberculosis, M. bovis,* and *M. africanum*, from all other mycobacteria. Except for *Mycobacteria leprae*, the other mycobacteria are referred to as atypical mycobacteria or nontuberculous mycobacteria (NTM).

It was proven that the inventive benzo[g]quinoxaline compounds of the present invention are effective agents for the prophylaxis and/or treatment of mycobacteria-induced infections. The following table illustrates the activity of selected benzo[g]quinoxaline derivatives against mycobacteria.

As shown in Tab. 1 the inventive benzo[g]quinoxaline derivatives exert their antiproliferative effect on *M. bovis* BCG and *M. tuberculosis* Erdmann at concentrations between <<1 µM and 32 µM. In contrast, growth of *E. coli* XI-1 blue was not affected by benzo[g]quinoxaline derivatives at concentrations higher than 10 µM. This demonstrates that the benzo[g]quinoxaline derivatives

specifically inhibit growth of mycobacteria. This also suggests that kinases which are completely lacking in *E.coli* are involved in mycobacterial proliferation.

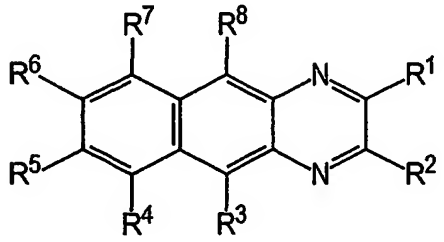


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Table 1: Growth inhibition of *M. bovis* BCG, *E. coli* XI-1 blue and *M. tuberculosis* Erdmann by benzo[g]quinoxaline derivatives.

Comp. No.	Inhibition [%] at 1µM	M.*bovis* Inhibition IC_{50} [µM]	M.*tuberculosis* Inhibition IC_{50} [µM]	*E.coli* Inhibition IC_{50} [µM]
14	54	0,9	10	>>10
15	46	1,2		>>10
16	8	18	20	>>10
17	96	<< 1		>>10
18	98	<< 1	10	>>10
32	99	32	8	>>10
21	56	7,7		>>10
201	100	<< 1	5	>>10
98	10			>>10
99	100	<< 1		>>10
398	21	12	10	>>10
365		0.3		
366		0.2		
363		< 0.1		
372		0.2		
373		< 0.1		
374		< 0.1		
377		0.3		
43		0.2		

44		0.2		
376		< 0.1		
83		0.5		
90		0.2		
95		0.3		
97		0.2		
116		0.3		
13		0.2	5	

The present invention provides also a method for preventing and/or treating mycobacteria-induced infections and diseases, including opportunistic infections, in a mammal, including a human, which comprises administering to the mammal an amount of at least one benzo[g]quinoxaline compound of the general formula (I) and/or a pharmaceutically acceptable salt thereof effective to prevent and/or treat mycobacteria-induced infections. Especially, these methods are used for the treatment of mycobacteria-induced infections like tuberculosis, leprosy or mycobacteria-induced meningitis.

Surprisingly, a number of other indications were found wherein the inventive benzo[g]quinoxaline derivatives could be applied successfully. The compound of the general formula (I) and/or pharmaceutically acceptable salts thereof can also be used for the prophylaxis and/or treatment of diabetes mellitus Type I and Type II, cancer, cancer cachexia, necrosis, gastric ulcers, neurodegenerative diseases (Alzheimer's disease, Parkinson's disease), influenza, multiple sclerosis, neuropathic diseases, neuropathic pain and polyneuropathy, neurological disorders, multiple sclerosis, Huntington's chorea, gastrointestinal ulcerative, inflammatory diseases and inflammations, peripheral and/or central nerve diseases, degradation of the peripheral and/or central nerve system, skin diseases, atopic eczema, psoriasis, urticaria and allergic reactions, rheumatoid arthritis, osteoarthritis, ulcerative colitis, Crohn's disease, ishemic diseases and ishemic heart disease, liver diseases and dysfunction of liver, cardiovascular diseases, psychiatric disorders, schizophrenia, alcoholism, attention deficit disorder, depression, obesity, stroke, pain, learning disabilities, senile macular degeneration, diseases affecting the immune system, impotence and male infertility, respiratory disorders, asthma and

infections and diseases mediated by infections of retroviruses, adenoviruses, hepadnaviruses, herpesviruses, influenza viruses and/or paramyxoviruses.

Thus, the present invention discloses the use of the benzo[g]quinoxaline derivatives as well as their application in various methods for preventing and/or treating infectious diseases, including opportunistic infections in a mammal, including a human. Said methods comprise the administration of at least one benzo[g]quinoxaline derivative or a salt thereof in an amount, effective to prevent and/or treat said infectious disease.

Furthermore, said benzo[g]quinoxalines or salts thereof can be used for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of the above mentioned diseases, especially infectious diseases and opportunistic diseases caused by viruses. Examples for such viruses are retroviruses (lentiviruses and oncoretroviruses), adenoviruses, hepadnaviruses, herpesviruses, influenza viruses and paramyxoviruses. Viruses which integrate in the genome of a cell are retroviruses, adenoviruses, herpesviruses and influenza viruses and sometimes hepadnaviruses while paramyxoviruses do not integrate in the genome of a cell are. Especially preferred is the use of the inventive benzo[g]quinoxaline compounds for the treatment of drug resistant virus strain.

The retroviruses may be selected from the group comprising lentiviruses and oncoretroviruses. Examples for lentiviruses are FIV, SIV, BIV, HIV-1, HIV-2, visna virus, caprine arthritis-encephalitis virus (CAEV), and equine infectious anemia virus (EIAV) as summarized in Table 2. Most preferably, the retrovirus represents the lentivirus HIV-1 or HIV-2. HTLV-I, HTLV-II and BLV belong to the oncoretroviruses. Furthermore, the excellent antiviral activity of the inventive benzo[g]quinoxaline compounds can preferably be used to treat retroviruses wherein the retrovirus is a T-cell tropic HIV strain or wherein the retrovirus is a macrophage-tropic HIV strain. Furthermore, the benzo[g]quinoxaline derivatives had successfully applied against a HIV-1 or HIV-2 strain which is resistant against protease inhibitors and/or reverse transcriptase inhibitors.

Table 2: Lentiviruses

Virus	Host	Diseases
EIAV	Horse	anemia, wasting
VMV	Sheep	pneumonia, wasting, arthritis, mastitis, encephalitis
CAEV	Goat	arthritis, mastitis, encephalitis
BIV	Cattle	none
FIV	Cat	immunodeficency, encephalitis, wasting
SIVs	various African monkey species	none
HIV-1, HIV-2	Humans	immunodeficency, pneumonia, encephalopathy, wasting, gastroenteropathy, nephropathy

SIV and FIV were discovered several years after HIV and the lesson that remains from the SIV and FIV studies is that lentiviruses alone in some circumstances are quite capable of causing slow immunosuppressive death.

In relation thereto, the present invention discloses a method for preventing and/or treating infections of retroviruses, especially HIV, in a mammal, including a human, which comprises administering to the mammal an amount of at least one benzo[g]quinoxaline compound and/or pharmaceutically acceptable salts thereof, effective to prevent and/or treat said retroviral infection, especially HIV.

Table 3 shows selected benzo[g]quinoxaline derivatives which have been tested as HIV inhibitors and their inhibition value.

Herein it is also revealed for the first time that the inventive benzo[g]quinoxaline compounds are potent HIV inhibitors. As shown in Table 3, the benzo[g]quinoxaline compounds are able to inhibit HI virus replication up to a value of 63% after 6 days at a concentration of 1 µM.

Table 3: Inhibitory effect of benzo[g]quinoxaline compounds on HIV replication.

Summary	Benzo[g]quinoxaline				
	No.	Compound	% inhibition of virus replication		
			d5 / 1µM	d5 / 100nM	d10 / 100nM
V47-BaL; PM1 inf. with HIV-1 BaL	1.	98	36	0	27
	2.	398	21	0	32
	3.	401	18	0	36
	4.	13	63 (d6)*	n.d.	45 (d6; 1µM)**
	5.	402	33	6	11
	6.	405	51	3	16
V47-NL4/3; PM1 inf. with HIV-1 NL4/3		Compound	% inhibition of virus replication		
			d5 / 1µM	d5 / 500nM	d10 / 500nM
	7.	98	40	n.d.	89
	8.	15	38	n.d.	77
	9.	17	55	n.d.	96
	10.	21	75	n.d.	97
	11.	398	69	n.d.	97
	12.	18	46	n.d.	97
	13.	401	56	n.d.	93
	14.	13	79 (d6)*	n.d.	72 (d6; 1µM)**
	15.	402	69	n.d.	93
	16.	403	63	n.d.	90
	17.	404	73	n.d.	97
	18.	405	54	n.d.	93

* measured after 6 days

** measured after 6 days at a concentration of 1 µM

Table 3 proves that the inventive benzo[g]quinoxaline compounds are higly potent HIV replication inhibitors and, therefore, can be used as pharmaceutically active agents in order to prevent and/or treat HIV infection.

Paramyxoviruses comprise respiratory syncytial virus, parainfluenza viruses, mumps virus, and measles virus. More preferably, the paramyxovirus is respiratory syncytial virus. The herpesvirus family comprises the human

herpesviruses 1 to 8 and different herpes viruses for various animal species as shown below in Table 4:

Table 4: Members of the herpesvirus family

Subfamily	Genus	Human	Animal
α-herpesvirus	simplex virus	human herpesvirus 1 (herpes simplex virus 1)	bovine herpesvirus 2
		human herpesvirus 2 (herpes simplex virus 2)	cercopithecine herpes-virus 1, (herpes B virus)
	varicella virus	human herpesvirus 3 (Varicella Zoster virus)	pseudorabiesvirus
			bovine herpesvirus 1
			equine-abortion virus
β-herpesvirus	cytomegalovirus	human herpesvirus 5 (HCMV)	
	muromegalovirus		murine herpesvirus 1
	roseolovirus	human herpesvirus 6, human herpesvirus 7	aotine herpesvirus 1, 3
γ-herpesvirus	lymphocrytovirus	human herpesvirus 4 (Epstein-Barr virus)	cercopithecine herpes-virus 2
			pongine herpesvirus 1
	rhadinovirus	human herpesvirus 8	ateline herpesvirus 2
			saimirine herpesvirus 1

More preferably, the herpesvirus is selected from Herpes simplex virus I, Herpes simplex virus II, Varicella Zoster virus, Epstein-Barr virus, HCMV, or HHV8. The hepadnavirus are selected from HBV, Ground-Squirrel-Hepatitis virus (GSHV), or Woodchuck hepatitis virus (WHV).

Table 5 shows a selected benzo[g]quinoxaline compound that is able to decrease the activity of the herpes viral target UL-97 for 75%. UL-97 is a validated target for herpes viral infections and it is known that a inhibition of UL-97 leads to an inhibition of the proliferation of human cytomegalo virus. Thus, the compounds of the present invention are useful as inhibitors for the herpes viral protein kinase UL-97.

Table 5: Inhibition of UL-97 activity by selected benzo[g]quinoxaline derivatives:

Comp. No.	Inhibition of UL-97 activity at 10 µM (% of DMSO control)
366	25

In relation thereto, a method for preventing and/or treating CMV in a mammal, including a human, is disclosed. That method comprises administering to the mammal an amount of at least one benzo[g]quinoxaline derivative and/or a pharmaceutically acceptable salt thereof which is effective to inhibit the herpes viral kinase UL-97.

Table 6 shows the inhibitory effect of selected benzo[g]quinoxaline derivatives on the HCMV target RICK.

Table 6: Inhibition of RICK activity by selected benzo[g]quinoxaline derivatives:

Comp. No.	Inhibition of RICK activity at 10 µM (% of DMSO control)
377	40
44	35
376	40
94	40
97	35

Another aspect of the present invention is directed to the use of the benzo[g]quinoxaline compounds for prophylaxis and/or treatment of influenza and to a method for preventing and/or treating influenza. As shown in Table 7, various benzo[g]quinoxaline derivatives are capable of inhibiting almost completely the replication of influenza viruses.

Table 7: Inhibition of influenza replication by selected benzo[g]quinoxaline derivatives:

Comp. No.	Influenza virus replication Inhibition [%] at 1 µM
363	100
378	100
377	100
81	100
83	100
116	80
13	100

The inventive compounds are also potent inhibitors for the human protein kinases SRPK1 and SRPK2. Said kinases play an important role in HBV infection. Thus, a method for preventing and/or treating HBV in a mammal, including a human, is disclosed. Said method comprises administering to the mammal an amount of at least one benzo[g]quinoxaline derivative and/or a pharmaceutically acceptable salt thereof, which is effective to inhibit the human protein kinase SRPK1 and/or SRPK2. From the results observed with compounds 13, 5, 369, 43 and 44, the class of benzo[g]quinoxalines is indicated to provide potent inhibitors of hepatitis B viral replication (cf. Table 8).

It was found that the inventive benzo[g]quinoxaline compounds and their salts are potent inhibitors for a variety of kinases and phosphatases, especially of protein kinases and phosphatases and most preferably of human protein kinases and phosphatases.

Table 8: Inhibition of HBV replication by selected benzo[g]quinoxaline derivatives:

Compound No.	EPR-signal (in % of DMSO control)	cellular toxicity (microscopical observ.)
13	8	no
5	33	no
369	23	no
43	7	no
44	5	no

Shown above are the effects of 20 µM concentrations of benzo[g]quinoxaline compounds on the levels of replication-competent cytoplasmic HBV particles measured in the endogeneous polymerase reaction (EPR). Significant reduction of the EPR signal was observed with the tested compounds. This finding indicates either a decrease in HBV polymerase activity or interference with HBV capsid assembly or pregenomic RNA encapsidation or with expression of viral RNA- or protein products in the HBV-expressing HepG2 2.2.15 hepatoma cell line.

A further aspect of the present invention relates to the use of a benzo[g]quinoxaline compound and/or a salt thereof for prophylaxis and/or treatment of TNF-α mediated diseases. In addition thereto a method for prophylaxis and/or treatment of TNF-α mediated diseases is disclosed. Said method comprises the administration of at least one benzo[g]quinoxaline derivative to a mammal, including a human, in need thereof, effective to treat and/or prevent said TNF-α mediated diseases.

TNF-α mediated diseases are summarized in WO 99/32110. Clinical studies have linked TNF-α production and/or signaling to a wide number of diseases including, for instance, rheumatoid arthritis, inflammatory and immunomodulatory diseases, such as acute rheumatic fever, bone resorption, postmenopausal osteoporosis, sepsis, gram negative sepsis, septic shock, endotoxic shock, toxic shock syndrome, systemic inflammatory response syndrome, inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, Jarisch-Herxheimer reactions, asthma, adult respiratory distress syndrome, acute pulmonary fobrotic diseases, pulmonary sarcoidosis, allergic respiratory diseases, silicosis, coal woker's pneumoconiosis, alveolar injury, hepatic failure, liver disease during acute inflammation, severe alcoholic hepatitis, malaria, non-insulin-depending diabetes mellitus, congestive heart failure, damage following heart disease, atherosclerosis, Alzheimer' disease, acute encephalitis, brain injury, multiple sclerosis, advanced cancer, lymphoid malignancies, pancreatitis, impaired wound healing in infection, inflammation and cancer, myelodysplastic syndromes, systemic lupus erythematosus, biliary cirrhosis, bowel necrosis, psoriasis, radiation injury, host-versus-graft reactions, such as ischemia reperfusion injury, allograft rejections of the kidney, liver, heart, lung and skin, tuberculosis, Helicobacter pylori infections during peptic ulcer disease, Chaga's disease, effects of Shiga-like toxin resulting from E. coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meninggococcal infection, infections from Borrelia burgdorferi,

Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis virus and human immunodeficiency virus.

Further testing of the inventive benzo[g]quinoxaline compound in relevant cellular systems revealed that they are also potent inhibitors of TNFα mRNA nuclear export. In addition thereto, it was surprisingly found that the benzo[g]quinoxaline compounds and/or pharmaceutically acceptable salts thereof act as inhibitors of nuclear export of TNF-α mRNA in TNF-α mediated diseases induced by bacteria and bacterial infections, respectively. A method had been established for regulating and/or inhibiting of nuclear export of TNF-α mRNA in TNF-α mediated diseases is disclosed, comprising administering a subject in need thereof a pharmaceutically effective amount of at least one benzo[g]quinoxaline compound and/or a pharmaceutically active salt thereof, effective to treat and/or regulate said nuclear export of TNF-α mRNA in TNF-α mediated diseases. Results are shown in Table 9. The selected benzo[g]quinoxaline compounds are highly potent inhibitors for TNF-α signaling and TNF-α mediated diseases.

Table 9: Inhibition of TNFα signaling by selected benzo[g]quinoxaline derivatives:

Comp. No.	TNFα signaling IC_{50} [μM]	Inhibition of TNFα signaling at 10 μM (% of DMSO control)
5	2	0
369	1	10
43	0.5	0
44	1	5
3	4	0
88	4	30
90	3	25
94	5	
97	4	0
116	4	0
13	10	20

A number of experiments revealed that the benzo[g]quinoxaline derivatives exhibit pharmaceutical activity for prophylaxis and/or treatment of a malignant diseases. Said malignant diseases comprise cancer, epithelial cell-derived tumor, a

monocytosis, a basal and squamous cell carcinoma, a hyperproliferating skin disease and psoriasis. The cancer is preferably selected from the group comprising bladder, breast, central nervous system, colon, gastric, lung, melanoma, head and neck, ovarian, cervix, glioblastoma, prostate, testis, leucemia, liver, and renal cancer. Targets for cancer treatment are, for instance, the protein kinases InsR, Abl, Akt, Adk1, PDGFR, and/or Src. Thus, the inventive benzo[g]quinoxaline derivatives can be used as inhibitors for the human protein kinases InsR, Abl, Akt, Adk1, PDGFR, and/or Src and a method for preventing and/or treating cancer in a mammal, including a human, is disclosed wherein said method comprises administering to the mammal an amount of at least one benzo[g]quinoxaline compound and/or pharmaceutically acceptable salts thereof effective to inhibit at least partially one of the human protein kinases Abl (2.7.1.112), Akt (2.7.1.-), Adk1, PDGFR (2.7.1.112), and/or Src (2.7.1.112).

Table 10 reveals that the inventive benzo[g]quinoxaline compounds are potent inhibitors for the prophylaxis and/or treatment of cancer. The cancer targets Akt, Abl, PDGFR and Src are inhibited with IC_{50} values between 0,3 and 16 µM.

Table 10: Inhibition of human cellular protein kinases know as cancer targets by selected benzo[g]quinoxaline derivatives:

Comp. No.	Cancer Target	Inhibition IC_{50} [µM]	Inhibition of activity at 10 µM (% of DMSO control)
99	Akt	0.03	100
363	Akt	10	48
369	Abl	0.3	3
369	Akt	1.3	7
369	PDGFR	12	36
369	Src	0.9	40
373	Akt	16	13
43	Abl	4.1	21
43	PDGFR	14	50
43	Src	3.6	47
44	Abl	1.8	1
44	Akt	1.2	2
44	PDGFR	7.1	23

44	Src	1.1	35
97	Abl	6.7	48
97	PDGFR	4.4	48

Another aspect is directed to a method for preventing and/or treating malignant diseases in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of general formula (I) and/or pharmaceutically acceptable salts thereof effective to prevent and/or treat said malignant disease. The malignant disease is selected from the group of diseases mentioned above.

Table 11 proves that the benzo[g]quinoxaline compounds are potent pharmaceutical agents for preventing and/or treating cancer.

Table 11: Cytotoxicity of selected benzo[g]quinoxaline derivatives measured in A549 and Jurkat cells.

Comp. No.	**A549 Inhibition IC_{50} [µM]**	**Jurkat Inhibition IC_{50} [µM]**
176	10	3
180	> 10	< 0.1
184	> 10	< 0.1
5	5	< 0.1
173	> 10	< 0.1
185	3	0.1
188	3	
191	> 10	< 0.1
385	5	3
365	> 10	3
363	3	< 0.1
378	> 10	3
369	10	1
44	> 10	2
376	> 10	2

88	5	3
90	5	1
91	> 10	1

The compounds of the present invention are also useful for the inhibition of cellular proliferation of cancer cells. A method for inhibiting cellular hyperproliferation of cancer cells was established. Said method comprises the administration of a pharmaceutically effective amount of at least one compound of the general formula (I) and/or pharmaceutically active salts thereof to a subject in need, effective to inhibit said cellular hyperproliferation of cancer cells.

Biological test reveal that the benzo[g]quinoxaline derivatives are also good pharmaceutically active agents for preventing and/or treating diabetes mellitus type I and/or diabetes mellitus type II in a mammal, including a human. A method was worked out, wherein a pharmaceutically active amount of at least one benzo[g]quinoxaline derivative was administered to a mammal, including a human, effective to activate the human protein kinase InsR. The insulin receptor InsR is a validated target for the treatment of diabetes mellitus type I and/or diabetes mellitus type II. Table 12 shows that the benzo[g]quinoxaline compounds of the present invention are able to activate the insulin receptor InsR and therefore can be used to treat diabetes mellitus type I and/or type II.

Table 12: Activation of the insulin receptor InsR by selected benzo[g]quinoxaline derivatives:

Comp. No.	Activation of InsR at 10 µM (% of DMSO control)
173	166
188	159
189	218

Because of the fact that the inventive benzo[g]quinoxaline compounds inhibit the human cellular protein kinase Akt which is also a known target for diabetes, the benzo[g]quinoxaline derivatives also act as pharmaceutically active agents for the treatment of diabetes mellitus type I and/or diabetes mellitus type II by inhibiting said kinase Akt.

Table 13: Inhibition of human cellular protein kinase Akt know as a target for diabetes by selected benzo[g]quinoxaline derivatives:

Comp. No.	Inhibition IC_{50} [µM]	Inhibition of activity at 10 µM (% of DMSO control)
363	10	48
369	1.3	7
373	16	13
44	1.2	2

Another aspect of the present invention relates to the use of the benzo[g]quinoxaline compound and/or a salt thereof for prophylaxis and/or treatment of HCV.

Tables 14 and 15 prove the activity of selected benzo[g]quinoxaline compounds against hepatitis C viruses.

Table 14: Effect of benzo[g]quinoxaline compounds on viability of Huh-5-2 replicon cells by the Alamar Blue toxicity assay.

conc. (µM)	compound 13 % of DMSO	compound 97 % of DMSO
20	106	98
10	117	108
5	116	113
2.5	117	118

Table 15: Effect of benzo[g]quinoxaline compounds on autonomous replication of HCV replicons in the Huh-5-2 cell line by luciferase reporter assay.

conc. (µM)	compound 13 % activity	compound 97 % activity
20	13	17
10	22	48
5	53	73
2.5	74	128

After normalization against background controls, mean values from the duplicate samples were expressed as percentage of the DMSO controls for the AlamarBlue (AB) as listed in Table 11 and luciferase reporter assays (luc) as listed in Table 12. The results are shown graphically in figure 8 and 9.

Toxicity was low for both compounds up to a concentration of 20 µM. Replication of subgenomic HCV replicon RNA as measured in the luciferase reporter assay was reduced for **compound 13** with an IC50 of 5 µM and for **compound 97** with an IC50 of 9 µM.

From the results observed with **compound 13** and **compound 97**, the class of benzo[g]quinoxalines is indicated to provide potent inhibitors of Hepatitis C viral replication.

Another aspect of the present invention is related to two novel targets for the treatment of HBV. Said two human protein kinases are known as SRPK1 and SRPK2 and have been validated as targets for the treatment of HBV and diseases associated with HBV infection.

Recent research has revealed how cells communicate with each other to coordinate the growth and maintenance of the multitude of tissues within the human body. A key element of this communication network is the transmission of a signal from the exterior of a cell to its nucleus, which results in the activation or suppression of specific genes. This process is called signal transduction.

An integral part of signal transduction is the interaction of ligands, their receptors and intracellular signal transduction molecules. Ligands are messengers that bind to specific receptors on the surface of target cells. As a result of the binding, the receptors trigger the activation of a cascade of downstream signaling molecules, thereby transmitting the message from the exterior of the cell to its nucleus. When the message reaches the nucleus, it initiates the modulation of specific genes, resulting in the production of RNA and finally proteins that carry out a specific biological function.

Disturbed activity of signal transduction molecules may lead to the malfunctioning of cells and disease processes. Specifically, interaction of HBV with host cells is necessary for the virus to replicate.

The present invention is also based upon the surprising fact that the human cellular protein kinases SR (serine/arginine-rich) protein-specific kinase 1 (SRPK1; Genbank accession number U09564) and SR protein-specific kinase 2 (SRPK2; Genbank accession number U88666/NM_003138) associate specifically with the HBV capsid protein and phosphorylate it. Published genetic analysis points to a role of core protein phosphorylation in essential steps of the HBV replication cycle (Nassal M. J Virol. 1992 Jul;66(7):4107-16; Lan YT, Li J, Liao W, and Ou J. Virology. 1999 Jul 5;259(2):342-8. Gazina EV, Fielding JE, Lin B and Anderson DA. J Virol. 2000 May;74(10):4721-8.). Therefore, inhibition of core protein phosphorylation through inhibition of the cellular kinase(s) involved is expected to interfere with virus replication. Thus, surprisingly it was found that the cellular kinases SRPK1 and SRPK2 interact with HBV core protein and will therefore interfere with virus replication. SRPK1 and SRPK2 constitute qualified targets for the indication Hepatitis B and allow the establishment of methods for the identification of compounds useful for prophylaxis and/or treatment of HBV infections and diseases induced by said infections, and allow directly the prophylaxis and treatment of HBV infections and associated diseases.

The antiviral therapeutic research approach described herein focuses on discovering the cellular signal transduction pathways involved in viral transfections. Identification of the signal transduction molecules that are key to viral infection provides for, among other things, novel targets for antiviral therapeutics, a novel class of antiviral therapeutics, and new screening methods (e.g., assays) and materials to find and develop new antiviral agents.

By screening of selected compounds in an SRPK2 kinase assay system, the small molecular weight compounds staurosporine from the class of indolocarbazoles, 3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic acid from the class of oxindoles, the compound roscovitine also known as 2-(*R*)-(1-ethyl-2-hydroxyethylamino)-6-benzylamino-9-isopropyl-purine from the class of purines, the compound 2,3-bis-(1*H*-indol-3-yl)-maleimide from the class of bisindolylmaleimides and rottlerin also known as (*E*)-1-[6-[(3-acetyl-2,4,6-trihydroxy-5-methylphenyl)methyl]-5,7-dihydroxy-2,2-dimethyl-2*H*-1-benzpropan-8-yl]-3-phenyl-2-propen-1-one as well as the inventive benzo[g]quinoxaline compounds of the general formula (I) were revealed as examples for inhibitors of the novel HBV target SRPK1 and SRPK2 and as anti-HBV compounds.

In order to develop new pharmaceutically active compounds, a potential target for medical intervention has to be identified. Thus, processes for finding pharmaceutically effective compounds include target identification.

Target identification is basically the identification of a particular biological component, namely a protein and its association with particular disease states or regulatory systems. A protein identified in a search for a pharmaceutically active chemical compound (drug) that can affect a disease or its symptoms is called a target. Said target is involved in the regulation or control of biological systems and its function can be interfered with by a drug.

Hepatitis B virus virions consist of viral capsids that contain the partially double-stranded DNA genome and are surrounded by envelopes made up of a host-cell derived lipid bilayer and the viral envelope proteins. The HBV capsid is composed of a single type of protein, the HBV core protein. The N-terminal 144 amino acids of core protein maintain the ability to self-assemble when expressed in heterologous systems, the 34 amino acid long C-terminus is arginine-rich and shows nonspecific binding to nucleic acids (reviewed in Nassal M. Hepatitis B virus morphogenesis, Curr. Top. Microbiol. Immunol. 1996, 214, 297-337). HBV core protein is a phospho protein (Machida A et al, J. Virol. 1991, 65(11), 6024-30; Lanford R.E., Notvall L, Virology 1990, 176(1), 222-33; Roossinck MJ, Siddiqui A. J Virol. 1987 Apr;61(4):955-61), and 3 phosphorylation sites have been identified in the arginine-rich C-terminus (S155, S162, S170 in subtype ayw; Liao W., Ou J.H. J. Virol. 1995, 69(2), 1025-9).

Genetic analysis points to a role of core protein phosphorylation at positions S155, S162 and S170 in HBV pregenomic RNA encapsidation or viral DNA synthesis, both essential steps of the HBV replication cycle (Nassal M, J. Virol. 1992, 66(7), 4107-16; Lan Y.T., Li J., Liao W., and Ou J., Virology 1999, 259(2), 342-8; Gazina E.V., Fielding J.E., Lin B. and Anderson D.AJ. Virol. 2000, 74(10), 4721-8). Therefore, inhibition of core protein phosphorylation through inhibition of the cellular kinase(s) involved is expected to interfere with virus replication. A kinase activity purified together with hepadnaviral core particles was first described in 1980 (Albin C., Robinson W.S J. Virol. 1980, 34(1), 297-302), however, the identity of this kinase or whether it is the cellular kinase that phosphorylates HBV core protein in vivo is not known. Kau and Ting (Kau JH, Ting LP J Virol. 1998 May;72(5):3796-803) identified a 46 kDa kinase that binds to and phosphorylates a GST-HBV core fusion protein and comigrates

with a core-particle associated kinase activity in an in-gel kinase assay, however, this cellular kinase was not further characterized.

Herein, the identification of SRPK1 (Genbank accession number U09564) and SRPK2 (Genbank accession number U88666/NM_003138) as the two major HBV-core associated cellular kinases is reported. Using an improved 16-BAC/SDS two-dimensional gel electrophoretic technique in combination with in-gel kinase assays, two GST-HBV core protein associated protein kinases could be detected which were capable of phosphorylating the HBV core protein in vitro. One of the distinct protein spots on the 2D gel was isolated and identified as SRPK1 by MALDI-TOF-MS analysis. This result was further confirmed by sequencing of selected tryptic peptides using a Q-TOF instrument for MS/MS analysis. The second associating protein kinase was identified as the related SRPK2 by immunoblot analysis. In vitro, both SRPK1 and SRPK2 phosphorylate HBV core protein on the same serine residues which have previously been identified as in-vivo phosphorylation sites. Moreover, moderate overexpression of either kinase correlates well with increased total cellular kinase activity towards HBV core protein in-vitro. Therefore SRPK1 and SRPK2 constitute qualified targets for the indication Hepatitis B and will allow testing for kinase-specific inhibitors in vitro.

Based on the surprising results reported herein, one aspect of the present invention is directed to a screening method for the identification of compounds useful for prophylaxis and/or treatment of HBV infections and/or diseases. Specifically, this method involves contacting a test compound with the human cellular protein kinase SRPK1 and/or SRPK2 and detecting the activity of said human cellular protein kinase SRPK1 and/or SRPK2.

Disclosed herein is the first report describing the role of human cellular kinases SRPK1 and SRPK2 in the signal transduction of the HBV infection process. As a result of these investigations, novel compounds and inhibitors against the above-mentioned kinases SRPK1 and SRPK2, such as the inventive benzo[g]quinoxalines, may be found by the use of the inventive methods disclosed herein.

It is apparent to a person skilled in the art that detection includes any method known in the art useful to indicate the presence, absence, or amount of a detection target. Such methods may include, but are not limited to, any

molecular or cellular techniques, used singularly or in combination, including, but not limited to: hybridization and/or binding techniques, including blotting techniques and immunoassays; labeling techniques (chemiluminescent, colorimetric, fluorescent, radioisotopic); spectroscopic techniques; separations technology, including precipitations, electrophoresis, chromatography, centrifugation, ultrafiltration, cell sorting; and enzymatic manipulations (e.g., digestion).

As used herein, the term "HBV induced" or "HBV associated" diseases refers to the group of diseases comprising chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.

Also described in the present invention are monoclonal or polyclonal antibodies which bind to the human cellular protein kinase SRPK1 and/or SRPK2.

A further aspect of the present invention relates to a method for preventing and/or treating HBV infections and/or associated diseases in an individual comprising the step of administering a pharmaceutically effective amount of an agent which inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or which inhibits at least partially the production of the human cellular protein kinase SRPK1 and/or SRPK2. Examples for the above-mentioned agents are the inventive benzo[g]quinoxaline compounds according to formula (I).

The term "individual" preferably refers to mammals, especially humans.

The methods disclosed herein can also be used for the treatment of hepatitis B virus strains resistant to current medications, in particular to nucleoside analog drugs like lamivudine. Lamivudine-resistant strains of HBV emerge upon prolonged treatment and are the primary cause of treatment failure (Fontaine H. et al., Letter, Ann. Intern. Med. 1999, 131, 716-717; Ling R. et al., Selection of mutations in the hepatitis B virus polymerase during therapy of transplant recipients with lamivudine, Hepatology 1996 24, 711-713). The most common lamivudine resistance mutations in HBV-infected patients, Met552Ile and Met552Val, appear at the Met (M) position in the highly conserved YMDD motif of the HBV polymerase and are frequently found in association with a second mutation, Leu528Met.

As used herein, the term "inhibitor" refers to any compound capable of downregulating, decreasing, suppressing or otherwise regulating the amount and/or activity of an enzyme, preferably a kinase or phosphatase, and most preferably a human protein kinase, such as SRPK1 and/or SRPK2. Generally, said inhibitors, including suicide inhibitors, may be proteins, oligo- and polypeptides, nucleic acids, genes, small chemical molecules, such as benzo[g]quinoxaline derivatives, or other chemical moieties.

Selected small molecular weight compounds from the classes of oxindoles, purines, indolocarbazoles, bisindolylmaleimides, especially staurosporine, 3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic, roscovitine, 2,3-bis-(1*H*-indol-3-yl)-maleimide, and rottlerin were found to inhibit SRPK2 kinase activity in a cellular assay. SRPK2 was overexpressed in eucaryotic cells, immunoprecipitated and incubated with test compounds before in-vitro kinase assays were performed.

Selected benzo[g]quinoxaline compounds as shown in Tables 16 and 17 have been identified as potent HBV replication inhibitors. Table 16 shows the inhibition of SRPK1 and Table 17 the inhibition of SRPK2.

Table 16: Effect of selected benzo[g]quinoxaline compounds on HBV replication

Comp. No.	SRPK1 Inhibition IC_{50} [µM]	Inhibition of SRPK1 at 10 µM (% of DMSO control)
176		30
182		37
183		41
173		44
369	5	31
44	1.8	9
83	7	39
97	11	53

Table 17: Effect of selected benzo[g]quinoxaline compounds on HBV replication

Comp. No.	SRPK1 Inhibition IC_{50} [µM]	Inhibition of SRPK1 at 10 µM (% of DMSO control)
44	11	50

Another aspect of the present invention is directed to a method for regulating the production and/or replication of HBV in an individual comprising the step of administering an individual a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or wherein said agent at least partially inhibits the production and/or replication of the human cellular protein kinase SRPK1 and/or SRPK2.

As used herein, the term "agent" refers to any chemical compound, such as a benzo[g]quinoxaline compound, capable of down- or upregulating, de- or increasing, suppressing, activating, stimulating or otherwise regulating the amount and/or activity of the human cellular protein kinase SRPK1 and/or SRPK2. Generally, said agents may be proteins, oligo- and polypeptides, nucleic acids, small chemical molecules, or other chemical moieties.

A similar aspect relates to a method for regulating the production and/or replication of HBV in cells comprising the step of administering the cells a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or wherein said agent at least partially inhibits the production of the human cellular protein kinase SRPK1 and/or SRPK2.

Monoclonal or polyclonal antibodies which bind to the human cellular protein kinase SRPK1 and/or SRPK2 may be used as effective agents within the above-mentioned methods.

As used herein, the term "regulating expression and/or activity" generally refers to any process that functions to control or modulate the quantity or activity (functionality) of a cellular component. Static regulation maintains expression and/or activity at some given level. Upregulation refers to a relative increase in expression and/or activity. Accordingly downregulation refers to a relative

decrease in expression and/or activity. Downregulation is synonymous with inhibition of a given cellular component's activity.

A further aspect is related to a method for regulating the expression of the human cellular protein kinase SRPK1 and/or SRPK2 in an individual comprising the step of administering the individual a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the transcription of DNA or the translation of RNA encoding SRPK1 or SRPK2.

And a still further aspect of the present invention relates to a method for regulating the expression of the human cellular protein kinase SRPK1 and/or SRPK2 in cells comprising the step of administering the cells a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the transcription of DNA or the translation of RNA encoding SRPK1 or SRPK2.

As used herein, a "pharmaceutical effective amount" of an inhibitor is an amount effective to achieve the desired physiological result, either in cells treated *in vitro* or in a subject treated *in vivo*. Specifically, a pharmaceutically effective amount is an amount sufficient to inhibit, for some period of time, one or more of the clinically defined pathological processes associated with the viral infection. The effective amount may vary depending on the specific inhibitor selected, and is also dependent on a variety of factors and conditions related to the subject to be treated and the severity of the infection. For example, if the inhibitor is to be administered *in vivo*, factors such as the age, weight and health of the patient as well as dose response curves and toxicity data obtained in pre-clinical animal work would be among those considered. If the inhibitor is to be contacted with the cells *in vitro*, one would also design a variety of pre-clinical *in vitro* studies to assess such parameters as uptake, half-life, dose, toxicity, etc. The determination of a pharmaceutically effective amount for a given agent is well within the ability of those skilled in the art.

A therapeutically effective amount or dosage of a compound, such as the inventive benzo[g]quinoxaline derivatives, staurosporine, 3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic, roscovitine, 2,3-bis-(1*H*-indol-3-yl)-maleimide, or rottlerin, refers to that amount of the compound that results in an at least partial inhibition of virus production in the patient, which may be measured in several ways, e.g., reduction in HBV DNA, HBe-Ag and HBs-Ag levels in the patient's serum, and/or improvement in alanine amino transferase

levels and liver histology and consequently results in a desired clinical benefit such as reduced viral load, suppression of progression of liver disease, and induction of immunological clearance or seroconversion. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical, pharmacological, and toxicological procedures in cell cultures or experimental animals for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effect is the therapeutic index and can be expressed as the ratio between LD50 and ED50. The dosage of the compound lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. Preferably, the dosage of the compound corresponds to an effective concentration in the range of 0.05 - 30 µM, more preferably in the range of 0.1 – 10 µM. The actual amount of the composition administered will be dependent on the subject being treated, on the subject's weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

The transcription of DNA and the translation of RNA can be inhibited by oligonucleotides or oligonucleotide derivatives. Thus, the present invention discloses oligonucleotides and derivatives of oligonucleotides which may be used in the above-mentioned methods. The oligonucleotide and/or its derivatives bind to the DNA and/or RNA encoding the human cellular protein kinase SRPK1 or SRPK2 and suppress the transcription of DNA or translation of RNA.

Some methods of the present invention identify compounds useful for prophylaxis and/or treatment of HBV infections and/or diseases induced by HBV infections by screening a test compound, or a library of test compounds, for its ability to inhibit the above-mentioned human cellular protein kinases SRPK1 and/or SRPK2. A variety of assay protocols and detection techniques are well known in the art and easily adapted for this purpose by a skilled practitioner. Such methods include, but are not limited to, high throughput assays (e.g., kinase assays), and *in vitro* and *in vivo* cellular and tissue assays.

The present invention incorporates by reference in their entirety techniques well known in the field of molecular biology. These techniques include, but are not limited to, techniques described in the following publications:
Ausubel, F.M. et al. eds., "Short Protocols In Molecular Biology" 4th Ed. 1999, John Wiley & Sons, NY (ISBN 0-471-32938-X);

Old, R.W. & S.B. Primrose "Principles of Gene Manipulation: An Introduction To Genetic Engineering" 3rd Ed. 1985, Blackwell Scientific Publications, Boston. Studies in Microbiology: V.2, 409 pp. (ISBN 0-632-01318-4);
Mayer, R.J. & J.H. Walker eds. "Immunochemical Methods In Cell and Molecular Biology" 1987, Academic Press, London. 325 pp. (ISBN 0-12480-855-7);
Winnacker, E.L. "From Genes To Clones: Introduction To Gene Technology" 1987 VCH Publishers, NY. (translated by Horst Ibelgaufts) 634 pp. (ISBN 0-89573-614-4).

In a further aspect the present invention relates to pharmaceutical compositions comprising at least one compound of the general formula (I) as an active ingredient together with one or more pharmaceutically acceptable carrier(s), excipient(s) or diluents.

The benzo[g]quinoxaline compounds of the present invention are basic and form pharmaceutically acceptable salts with organic and inorganic acids. Examples of suitable acids for such acid addition salt formation are hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, acetic acid, citric acid, oxalic acid, malonic acid, salicylic acid, p-aminosalicylic acid, malic acid, fumaric acid, succinic acid, ascorbic acid, maleic acid, sulfonic acid, phosphonic acid, perchloric acid, nitric acid, formic acid, propionic acid, gluconic acid, lactic acid, tartaric acid, hydroxymaleic acid, pyruvic acid, phenylacetic acid, benzoic acid, p-aminobenzoic acid, p-hydroxybenzoic acid, methanesulfonic acid, ethanesulfonic acid, nitrous acid, hydroxyethanesulfonic acid, ethylenesulfonic acid, p-toluenesulfonic acid, naphthylsulfonic acid, sulfanilic acid, camphorsulfonic acid, china acid, mandelic acid, o-methylmandelic acid, hydrogen-benzenesulfonic acid, picric acid, adipic acid, d-o-tolyltartaric acid, tartronic acid, α-toluic acid, (o, m, p)-toluic acid, naphthylamine sulfonic acid, and other mineral or carboxylic acids well known to those skilled in the art. The salts are prepared by contacting the free base form with a sufficient amount of the desired acid to produce a salt in the conventional manner.

It is also possible to obtain acid addition salts with amino acids like methionine, tryptophane, lysine or arginine, especially with benzo[g]quinoxaline compounds of the general formula (I) carrying a carboxylic acid residue.

Depending upon the substituents on the inventive benzo[g]quinoxaline compounds, one may be able to form salts with bases, too. Thus, for example,

if there are carboxylic acid substituents in the molecule, salts may be formed with inorganic as well as organic bases such as, for example, NaOH, KOH, NH_4OH, tetraalkylammonium hydroxide, and the like.

The compounds of the general formula (I) can also be administered in form of their pharmaceutically active salts optionally using substantially nontoxic pharmaceutically acceptable carriers, excipients or diluents. The medications of the present invention are prepared in a conventional solid or liquid carrier or diluents and a conventional pharmaceutically-made adjuvant at suitable dosage level in a known way. The preferred preparations are in administratable form which is suitable for oral application. These administratable forms, for example, include pills, tablets, film tablets, coated tablets, capsules, powders and deposits.

Furthermore, the subject of the present invention also includes pharmaceutical preparations for parenteral, including dermal, intradermal, intragastrical, intracutaneous, intravasal, intravenous, intramuscular, intraperitoneal, intranasal, intravaginal, intrabuccal, percutaneous, rectal, subcutaneous, sublingual, topical or transdermal application, which in addition to typical vehicles and diluents contain a benzo[g]quinoxaline compound of the general formula (I) and/or a pharmaceutically acceptable salt thereof as active ingredient.

Within the disclosed methods the pharmaceutical compositions of the present invention, containing benzo[g]quinoxaline derivatives of the general formula (I) as active ingredients, will typically be administered in admixture with suitable carrier materials selected with respect to the intended form of administration, i.e. oral tablets, capsules (either solid-filled, semi-solid filled or liquid filled), powders for constitution, oral gels, elixirs, dispersible granules, syrups, suspensions, and the like, and consistent with conventional pharmaceutical practices. For example, for oral administration in the form of tablets or capsules, the active drug component may be combined with any oral nontoxic pharmaceutically acceptable inert carrier, such as lactose, starch, sucrose, cellulose, magnesium stearate, dicalcium phosphate, calcium sulfate, talc, mannitol, ethyl alcohol (liquid forms) and the like. Moreover, when desired or needed, suitable binders, lubricants, disintegrating agents and coloring agents may also be incorporated in the mixture. Powders and tablets may be comprised of from about 5 to about 95 percent inventive composition.

Suitable binders include starch, gelatin, natural sugars, corn sweeteners, natural and synthetic gums such as acacia, sodium alginate, carboxymethylcellulose, polyethylene glycol and waxes. Among the lubricants, there may be mentioned for use in these dosage forms, boric acid, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrants include starch, methylcellulose, guar gum and the like. Sweetening and flavoring agents and preservatives may also be included where appropriate. Some of the terms noted above, namely disintegrants, diluents, lubricants, binders and the like, are discussed in more detail below.

Additionally, the compositions of the present invention may be formulated in sustained release form to provide the rate controlled release of any one or more of the components or active ingredients to optimize the therapeutic effects, i.e. antihistaminic activity and the like. Suitable dosage forms for sustained release include layered tablets containing layers of varying disintegration rates or controlled release polymeric matrices impregnated with the active components and shaped in tablet form or capsules containing such impregnated or encapsulated porous polymeric matrices.

Liquid form preparations include solutions, suspensions and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injections or addition of sweeteners and opacifiers for oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions for intranasal administration.

Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be in combination with a pharmaceutically acceptable carrier such as inert compressed gas, e.g. nitrogen.

For preparing suppositories, a low melting wax such as a mixture of fatty acid glycerides such as cocoa butter is first melted, and the active ingredient is dispersed homogeneously therein by stirring or similar mixing. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool and thereby solidifies.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

The inventive benzo[g]quinoxaline compounds of the present invention may also be deliverable transdermally. The transdermal compositions may take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or reservoir type as are conventional in the art for this purpose.

The term capsule refers to a special container or enclosure made of methyl cellulose, polyvinyl alcohols, or denatured gelatins or starch for holding or containing compositions comprising the active ingredients. Hard shell capsules are typically made of blends of relatively high gel strength bone and pork skin gelatins. The capsule itself may contain small amounts of dyes, opaquing agents, plasticizers and preservatives.

Tablet means compressed or molded solid dosage form containing the active ingredients with suitable diluents. The tablet can be prepared by compression of mixtures or granulations obtained by wet granulation, dry granulation or by compaction well known to a person skilled in the art.

Oral gels refers to the active ingredients dispersed or solubilized in a hydrophillic semi-solid matrix.

Powders for constitution refers to powder blends containing the active ingredients and suitable diluents which can be suspended in water or juices.

Suitable diluents are substances that usually make up the major portion of the composition or dosage form. Suitable diluents include sugars such as lactose, sucrose, mannitol and sorbitol, starches derived from wheat, corn rice and potato, and celluloses such as microcrystalline cellulose. The amount of diluents in the composition can range from about 5 to about 95% by weight of the total composition, preferably from about 25 to about 75%, more preferably from about 30 to about 60% by weight.

The term disintegrants refers to materials added to the composition to help it break apart (disintegrate) and release the medicaments. Suitable disintegrants include starches, "cold water soluble" modified starches such as sodium carboxymethyl starch, natural and synthetic gums such as locust bean, karaya, guar, tragacanth and agar, cellulose derivatives such as methylcellulose and

sodium carboxymethylcellulose, microcrystalline celluloses and cross-linked microcrystalline celluloses such as sodium croscarmellose, alginates such as alginic acid and sodium alginate, clays such as bentonites, and effervescent mixtures. The amount of disintegrant in the composition can range from about 2 to about 20% by weight of the composition, more preferably from about 5 to about 10% by weight.

Binders characterize substances that bind or "glue" powders together and make them cohesive by forming granules, thus serving as the "adhesive" in the formulation. Binders add cohesive strength already available in the diluent or bulking agent. Suitable binders include sugars such as sucrose, starches derived from wheat, corn rice and potato; natural gums such as acacia, gelatin and tragacanth; derivatives of seaweed such as alginic acid, sodium alginate and ammonium calcium alginate; cellulosic materials such as methylcellulose and sodium carboxymethylcellulose and hydroxypropylmethylcellulose; polyvinylpyrrolidone; and inorganics such as magnesium aluminum silicate. The amount of binder in the composition can range from about 2 to about 20% by weight of the composition, more preferably from about 3 to about 10% by weight, even more preferably from about 3 to about 6% by weight.

Lubricant refers to a substance added to the dosage form to enable the tablet, granules, etc. after it has been compressed, to release from the mold or die by reducing friction or wear. Suitable lubricants include metallic stearates such as magnesium stearate, calcium stearate or potassium stearate; stearic acid; high melting point waxes; and water soluble lubricants such as sodium chloride, sodium benzoate, sodium acetate, sodium oleate, polyethylene glycols and D,L-leucine. Lubricants are usually added at the very last step before compression, since they must be present on the surfaces of the granules and in between them and the parts of the tablet press. The amount of lubricant in the composition can range from about 0.2 to about 5% by weight of the composition, preferably from about 0.5 to about 2%, more preferably from about 0.3 to about 1.5% by weight.

Glidents are materials that prevent caking and improve the flow characteristics of granulations, so that flow is smooth and uniform. Suitable glidents include silicon dioxide and talc. The amount of glident in the composition can range from about 0.1% to about 5% by weight of the total composition, preferably from about 0.5 to about 2% by weight.

Coloring agents are excipients that provide coloration to the composition or the dosage form. Such excipients can include food grade dyes and food grade dyes adsorbed onto a suitable adsorbent such as clay or aluminum oxide. The amount of the coloring agent can vary from about 0.1 to about 5% by weight of the composition, preferably from about 0.1 to about 1%.

Yet another aspect of the present invention is directed to pharmaceutical compositions useful for the prophylaxis and/or treatment of an individual afflicted with HBV comprising at least one agent, such as the inventive benzo[g]quinoxaline compounds, capable of inhibiting at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2.

Still another aspect of the present invention relates to pharmaceutical compositions comprising a further active ingredient selected from the group comprising pharmaceutically active compounds and/or their pharmaceutically acceptable salts, such as lamivudine ((-)-β-L-2',3'-dideoxy-3'-thiacytidine marketed as e.g., Zeffix®, Heptovir®, 3TC®, Epivir-HBV, Combivir®, Trizivir® by GlaxoSmithKline), alpha interferon (e.g., Intron A® by Schering-Plough), FTC (e.g., Coviracil® by Triangle Pharmaceuticals), DAPD (DXG, by Triangle), L-FMAU (e.g., Clevudine® by Triangle), Adefovir dipivoxil (by Gilead Sciences), tenofovir, epavudine, epcitabine, lobucavir, Penciclovir (GlaxoSmithKline), Entecavir/BMS-200475 (by Bristol-Myers Squibb), Racivir (by Pharmasset), L-ddA prodrug, HDP-P-acyclovir, ara-AMP prodrugs, thymosin alpha-1 (e.g., Zadaxin® by SciClone), (-)-Carbovir, hammerhead ribozymes, HBV DNA vaccine such as Genevax® (by Wyeth-Lederle Vaccine), PreS1/S2 vaccine (e.g., Hepagene® by Medeva PLC), HBV immunoglobulin (e.g., Nabi-HBV® by Nabi), glycosidase inhibitors such as Nonyl-DNJ (by Synergy), human monoclonal antibodies directed against HBV (e.g., by XTL Biopharmaceuticals) and any other antiviral composition in use or in development for use to treat hepatitis B infection.

A further aspect of the present invention describes a combination therapy, wherein an SRPK1 inhibitor and/or SRPK2 inhibitor, such as staurosporine, 3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic, roscovitine, 2,3-bis-(1*H*-indol-3-yl)-maleimide, or rottlerin is administered in combination with further therapeutic compounds. Preferably said further therapeutic compounds are chosen from the group of hepatitis B virus drugs or vaccines comprising

lamivudine ((-)-β-L-2',3'-dideoxy-3'-thiacytidine marketed as e.g., Zeffix®, Heptovir®, 3TC®, Epivir-HBV, Combivir®, Trizivir® by GlaxoSmithKline), alpha interferon (e.g., Intron A® by Schering-Plough), FTC (e.g., Coviracil® by Triangle Pharmaceuticals), DAPD (DXG, by Triangle), L-FMAU (e.g., Clevudine® by Triangle), Adefovir dipivoxil (by Gilead Sciences), tenofovir, epavudine, epcitabine, lobucavir, Penciclovir (GlaxoSmithKline), Entecavir/BMS-200475 (by Bristol-Myers Squibb), Racivir (by Pharmasset), L-ddA prodrug, HDP-P-acyclovir, ara-AMP prodrugs, thymosin alpha-1 (e.g., Zadaxin® by SciClone), (-)-Carbovir, hammerhead ribozymes, HBV DNA vaccine such as Genevax® (by Wyeth-Lederle Vaccine), PreS1/S2 vaccine (e.g., Hepagene® by Medeva PLC), HBV immunoglobulin (e.g., Nabi-HBV® by Nabi), glycosidase inhibitors such as Nonyl-DNJ (by Synergy), human monoclonal antibodies directed against HBV (e.g., by XTL Biopharmaceuticals) and any other antiviral composition in use or in development for use to treat hepatitis B infection.

It is readily apparent to those skilled in the art that other suitable modifications and adaptations of the compositions and methods of the invention described herein are evident and may be made without departing from the scope of the invention or the embodiments disclosed herein. Having now described the present invention in detail, the same will be more clearly understood by reference to the following examples, which are included for purposes of illustration only and are not intended to be limiting of the invention.

Description of figures

Fig. 1 shows that all three GST-HBV core fusion proteins were phosphorylated in an in-vitro kinase assay.

Fig. 2 shows a 45 kDa kinase detected in the total cell lysate that phosphorylates GST-HBV-C1, but which is not found to be significantly associated with the GST-HBV core fusion proteins.

Fig. 3 shown an in-gel kinase assay with GST-HBV-C1 as substrate, in order to identify the protein spots representing the specifically associated kinases.

Fig. 4 shows that the transfection of either FLAG-SRPK1 or SRPK2-VSV expression plasmids into cells leads to increased levels of specifically GST-HBV-C1-associating SRPK1 or SRPK2.

Fig. 5 shows that mutation of all three serines to alanines strongly reduced HBV core protein phosphorylation in cells.

Fig. 6 shows that both SRPK1 and SRPK2 exhibit the same substrate specificity in-vitro as the cellular kinases in-vivo.

Fig. 7 shows that the overexpression of either SRPK1 or SRPK2 correlates with increased GST-HBV-C1 phosphorylation by total cellular proteins in-vitro.

Fig. 8 shows the effects of various concentrations of the benzo[g]quinoxaline compound No. 13 on autonomous replication of subgenomic HCV replicons in the Huh-5-2 replicon cell line.

Fig. 9 shows the effects of various concentrations of the benzo[g]quinoxaline compound No. 97 on autonomous replication of subgenomic HCV replicons in the Huh-5-2 replicon cell line.

Examples

Analytical Methods

HPLC-MS

LC-MS analyses were performed by Waters chromatograph/ ZMD mass spectrometer equipped with Waters 996 DAD UV detector Waters 2700 autosampler and Waters 600 controller.

Supelco Discovery RP-AmideC16 column was used in gradient mode at 3ml/min flow rate.

Initial solvent: 10% AcCN/ 90% Water/ 0.05% HCOOH. Solvent B: 100% AcCN

Gradient: 0% B till 30 sec, 0-80% between 30-120sec, 80% till 240sec, 80-0% between 240-260 sec, 0% till 360 sec.

Injection: 5µg

Solvents were purchased from Riedel-deHaën company (Acetonitrile G Chromasolv (34998)

Formic Acid extra pure (27001)) Distilled water was purified by Mili-Q Academic equipment.

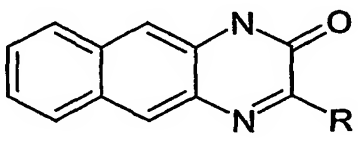
Details of mass spectrometry: Ionization: ES+/ES-, Source block temp: 120°C Desolvation temp: 350°C Desolvation Gas: 400 L/min Cone Gas: 100 L/min Capillary: 3000 V Cone: 25 V

Extractor: 3 V Rf Lens: 0.2 V Scan: 120 to 1000 m/z in 1 sec Inter-scan delay: 0.1 s

NMR

300 MHz H^1-NMR analyses were performed by Bruker AC-300 equipment at 25°C. DMSO $-d_6$ was generally used as solvent while the exceptions are given.

Example 1



R= H, 2-thienyl

(Compound 1) 1,4-Dihydro-benzo[g]quinoxaline-2-one (1*H*-benzo[g]quinoxaline-2-one)

3.32 g (20 mmol) 2,3-diaminonaphthalene was dissolved in the mixture of 5 ml DMF and 50 ml ethanol. 5 ml aqueous solution (50%) of glyoxalic acid was added and the mixture was stirred for 2 hours at reflux temperature. The reaction mixture was cooled to room temperature and the product was filtered, washed two times with diethyl ether and dried.

Yield: 3.5 g (90%)

Rt: 2.76 min.; Mol. Mass: 196

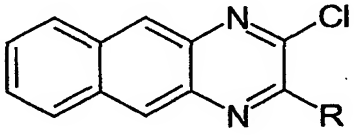
(Compound 2) 1,4-Dihydro-2-(2-thienyl)-benzo[g]quinoxaline-3-one (3-Thiophen-2-yl-1*H*-benzo[g]quinoxaline-2-one)

3.32 g (20 mmol) 2,3-diaminonaphthalene was dissolved in the mixture of 5 ml DMF and 50 ml ethanol. 5 ml aqueous solution (50%) of glyoxalic acid was added and the mixture stirred for 2 hours at reflux temperature. The reaction mixture was cooled to room temperature and the product was filtered, washed two times with diethyl ether and dried.

Yield: 3.61 g (65%)

Rt: 3.34 min.; Mol. Mass: 278

Example 2



R= H, Cl, 2-thienyl

(Compound 3) 2-Chloro-benzo[g]quinoxaline

1.1 g (5 mmol) benzo[g]quinoxalin-2-one was suspended in 30 ml dry phosphorus oxychloride, 0.3 ml DMF was added and refluxed for 3 hours in a flask equipped with cooler stopped with $CaCl_2$ tube. Phosphorus oxychloride was removed in vacuum and the residue was mixed with crushed ice and ethyl acetate. Then saturated solution of sodium hydrocarbonate was added and the mixture was shaken in a separatory funnel. The extraction was repeated 3 times and organic phases were collected and dried on sodium sulfate and evaporated.

Yield: 890 mg (82%)

Rt: 3.17 min.; Mol. Mass: 214

δ (ppm) = 8.98(s, 1H, 3-H), 8.84(s, 1H, 5-H), 8.71(s, 1H, 10-H), 8.28(m, 2H, 6,9-H), 7.71(m, 2H, 7,8-H)

(Compound 4) 2-(2-Thienyl)-3-chloro-benzo[g]quinoxaline

The reaction procedure is similar to that for Compound 3. Instead of 1*H*-benzo[g]quinoxaline-2-one the compound 3-Thiophen-2-yl-1*H*-benzo[g]quinoxaline-2-one was used.

Yield: 1 g (69%)

Rt: 3.85 min.; Mol. Mass: 298

(Compound 5) 2,3-Dichloro-benzo[g]quinoxaline

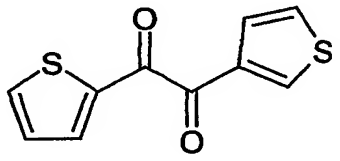
5.45 g (0.029 mol) of 1,4-dihydro-benzo[g]quinoxaline-2,3-dione was refluxed in 58.7 ml (0.641 mol) phosphorus oxychloride. The reaction was catalyzed with 0.40 g (3.3 mmol) of 4-dimethylaminopyridine. After 4 hours of boiling the mixture was poured onto ice and water and the formed precipitate was filtered off, washed with water and dried under vacuum. Purified by chromatography using ethyl acetate eluent.

Yield: 77%

Rt: 3.41min.; Mol. Mass: 249

δ (ppm) = 8.76(s, 2H, 5,10-H), 8.26(m, 2H, 6, 9-H), 7.72(m, 2H, 7, 8-H)

Example 3



(Compound 6) 2,3-Thenil

a) Thiophenecarboxanilide

A mixture of thiophene-2-carbonyl chloride (5 ml. 46.6 mmol), and aniline (4.7 ml, 51.3 mmol) in chloroform is cooled to 0^0C, then triethyl amine (7.2 ml, 52 mmol) was added dropwise. The mixture was stirred at room temperature for two hours. The solid residue was extracted with chloroform and water. The organic layer was separated, dried on Na_2SO_4, and evaporated to dryness.

Rt: 2.98 min.; Mol. Mass: 203

b) Imidoyl chloride

A mixture of the above material (10.04 g, 49.3 mmol), and phosphorus pentachloride (11.2 g, 53.72 mmol) in benzene was refluxed overnight, then cooled to room temperature. The reaction mixture was placed into a distillation apparatus and the solvent was removed in vacuum. The pressure was reduced to 1.5 mmHg, and the temperature of the oil-bath was raised slowly. N-phenylthiophene-2-carbimidoyl chloride distilled as yellow oil.

The substace obtained in this way was used without analysis because of its instability.

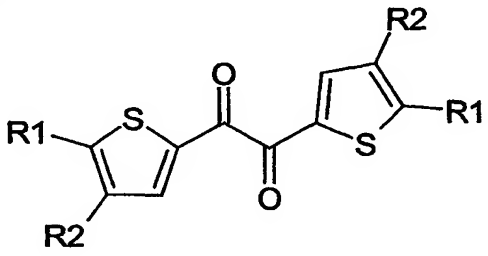
c) Thenil

A mixture of the imidoyl chloride (6.81 g, 30.7 mmol) freshly distilled 3-thiophene-carboxaldehyde (2.24 ml 33.8 mmol), dimethylimidazolium iodide (2.27 g, 10 mmol) and sodium hydride (1.3 g, 54.1 mmol) in anhydrous (abs.) tetrahydrofurane (THF) (220 ml) is heated at the reflux temperature overnight, then poured on ice. The mixture is extracted with ethyl acetate and water. The organic layer was separated, dried on Na_2SO_4, and concentrated. The black oil is chromatographed on silica column with chloroform.

Rt: 3.04 min.; The calculated molecular mass is 297 but the measured one was 194 because of the decomposition of thenil during ionisation.

δ (ppm) = 8.64(dd, 1H, 2'-H 4J=1.2 Hz), 8.28(dd, 1H, 5'-H, ^{3}J=4.9Hz), 7.93(dd, 1H, 5-H, ^{3}J=3.9Hz, 4J=1.3Hz), 7.77(dd, 1H, 3-H, ^{3}J=4.7Hz), 7.63(dd, 1H, 4'H), 7,33(dd, 1H, 4-H)

Example 4



R1 or R2 alternatively = H or (CH2)nCOO(CH2)n-H, n=0-6

General Procedure for Compound 7-10

A mixture of methyl or ethyl ω-thienyl alkylcarboxylates (24.5 mmol) and oxalyl chloride (8 ml, 27 mmol) in dichloromethane (73 ml) is cooled to –78^{0}C then (54.7 mmol) $AlCl_3$ was added to the mixture in portions, then stirred at room temperature for overnight then poured in the mixture of ice and HCl. After stirring for 20 min. the mixture was extracted with ethylacetate. The organic

layer was separated, dried on Na_2SO_4, and concentrated. The residue was dissolved in ethyl acetate chromatographed on Al_2O_3 column in ethyl acetate eluent.

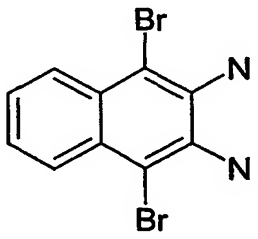
(Compound 7) Bis(4,4'-methoxycarbonylmethyl)-2,2'-thenil
Rt: 3.11; Mol. Mass: 366

(Compound 8) Bis(5,5'-methoxycarbonylmethyl)-2,2'-thenil
Rt: 3.12; Mol. Mass: 366

(Compound 9) Bis(4,4'-ethoxycarbonylpropyl)-2,2'-thenil
Rt: 3.41; Mol. Mass: 450

(Compound 10) Bis(5,5'-methoxycarbonylethyl)-2,2'-thenil
Bis(5,5'-methoxycarbonylethenyl)-2,2'-thenil was synthesized from 2-thienilacrylic acid methyl ester according to the general method given above.
Rt: 3.09 Mol Mass: 390
Double bonds were saturated with hydrogen in ethanol solvent in presence of 10% palladium catalyst on charcoal.
Rt: 3.19 Mol. Mass: 394

Example 5 1,4-Dibromo-naphthalene-2,3-diamine



(Compound 11) 1,4-dibromo-2,3-diaminonaphthalene
The solution of 3.2 g (1.02 ml, 20 mmol) bromine in 250 ml glacial acetic acid was added for 2 days to 1.58 g (10 mmol) naphthalene-2,3-diamine, and 1.80 g sodium acetate in 100 ml acetic acid (glacial) with dropwise. The mixture was stirred for 1 day, then 10 ml water was added, filtrated, and the solution diluted with 500 ml water.

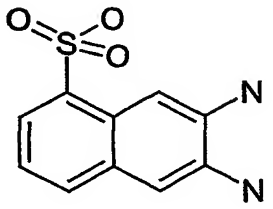
The precipitate was filtered off, and washed with 50 ml water and 50 ml n-hexane.

Yield: 1.72 g (55%)

Rt: 3.32 min.; Mol. Mass: 316

δ (ppm) = 7.80(m, 2H, 5,8-H), 7.29(m, 2H, 6,7-H), 5.68(s, 4H, NH_2)

Example 6



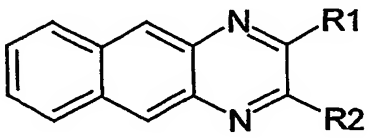
(Compound 12) 2,3-Diaminonaphthalene 5-sulfonic acid sodium salt

50 ml concentrated (cc.) sulphuric acid was placed into a flask equipped with $CaCl_2$ tube, dropping funnel and thermometer. The apparatus was cooled in ice and 50 ml chlorosulphonic acid was dropped in with vigorous stirring while temperature was kept under 5 degrees. 7.9 g (50 mM) 2,3-diaminonaphthanele was slowly added in portions. After two hours of stirring at room temperature the reaction mixture was poured on ice. The crystals formed were filtrated off and washed with cold water and dried over sulphuric acid in vacuum.

Yield: 11.8g (100%)

δ (ppm) = 8.15(s, 2H, 5-H), 7.82(d, 1H, 9-H, ^3J=7.2 Hz), 7.78(d, 1H, 7-H, ^3J=8.2Hz), 7.54(s,1H, 2-H, 10-H), 7.32(t, 1H, 8-H), 7.26(bs, 1H, OH), 6.58(bs, 4H, NH_2)

Example 7



R1, R2= H, alkyl, aryl

General Procedure for Compound 13-30

2,3-Diaminonaphthalene (or its derivative) was dissolved in the mixture of 1 ml DMF and 3 ml ethanol with gentle warming. After dissolving of the amine it was cooled to room temperature and the solution of oxo compound (glyoxales or 1,2 diketones) in 1 ml ethanol was added with stirring. The reaction mixture was refluxed for 1 hour then allowed to cool to room temperature while the product crystallized. Crystals were collected by filtration, washed with ether and dried in vacuum.

(Compound 13) 2,3-Bis-(2-thienyl)-benzo[g]quinoxaline

Rt: 3.71 min; Mol. Mass: 344

δ (ppm) = 8.72(s, 2H, 5,10-H), 8.23(m, 2H, 6,9-H), 7.85(d, 2H, 5'-H, ^{3}J =4.82Hz), 7.64(m, 1H, 2-H, 7,8-H), 7.28(d, 2H, 3'-H, ^{3}J =3.5 Hz), 7.14(dd, 2H, 4'-H)

(Compound 14) 2-Phenyl-benzo[g]quinoxaline

Rt: 3.55 min; Mol. Mass: 256

δ (ppm) = 9.65(s, 1H, 2-H), 8.81(s, 1H, 5-H), 8.80(s, 1H, 10-H), 8.41(m, 2H, 2',6'-H), 8.26(m, 2H, 6,9-H), 7.64(m, 5H, 7,8,3',4',5'-H)

(Compound 15) 2-para-Tolylbenzo[g]quinoxaline

Rt: 2.75 min; Mol. Mass: 270

δ (ppm) = 9.63(s, 1H, 5-H), 8.78(s, 1H, 10-H), 8.33(d, 2H, 2',6'-H, ^{3}J=8.5Hz), 8.25(m, 2H, 6,9-H), 7.66(m, 2H, 7,8-H), 7.45(d, 2H, 3'5'-H), 2.43 (s, 3H)

(Compound 16) 2-(3-Chlorophenyl)-benzo[g]quinoxaline

Rt: 3.79 min; Mol. Mass: 291

δ (ppm) = 9.64(s, 1H, 3-H), 8.84(s, 1H, 5-H), 8.80(s, 1H, 10-H), 8.43(s,1H, 2'-H), 8.36(m, 1H, 5'-H), 8.27(m, 2H, 6,9-H), 7.67(m, 4H, 7,8,4',6'-H)

(Compound 17) 2-(4-Chlorophenyl)-benzo[g]quinoxaline

Rt: 3.87 min; Mol. Mass: 290

δ (ppm) = 9.65(s, 1H), 8.80(s, 2H), 8.44(d, 2H), 8.26(m, 2H), 7.66(m, 4H)

(Compound 18) 2-(4-Bromophenyl)-benzo[g]quinoxaline

Rt: 3.92 min; Mol. Mass: 335

δ (ppm) = 9.64(s, 1H, 2-H), 8.80(s, 1H, 5-H), 8.79(s, 1H, 10-H), 8.36(d, 2H, 2',6'-H, ^{3}J=8.5Hz), 8.25(m, 2H, 6,9-H), 7.83(d, 2H, 3',5'-H), 7.66 (m, 2H)

(Compound 19) 2-Adamantan-2-yl-benzo[g]quinoxaline
Rt: 3.83 min; Mol. Mass: 314
δ (ppm) = 9.06(s, 1H), 8.98(s, 1H), 8.87(s, 1H), 8.30(m, 2H), 7.70(s, 2H), 1.98-1.18(m, 14H, adamantine)

(Compound 20) 2,3-Dipyridyl-2-yl-benzo[g]quinoxaline
Rt: 3.02 min; Mol. Mass: 334
δ (ppm) = 8.89(s, 2H, 5,10-H), 8.29(m, 4H, 6,9,6'-H), 8.01(d, 2H, 3'-H, ^{3}J=7.7Hz), 7.89(t, 2H, 5'-H, ^{3}J=6.7Hz), 7.70(m, 2H, 7,8-H), 7.37(t, 2H, 4'-H)

(Compound 21) 2,3-Diphenylbenzo[g]quinoxaline
Rt:3.81 min; Mol. Mass: 332
δ (ppm) = 9.83(s, 2H, 5,10-H), 8.27(m, 2H, 6,9-H), 7.66(m, 2H, 7,8-H), 7.53(m, 4H, 2',6'-H), 7.45-7.35(m, 6H, 3',4',5'-H)

(Compound 22) 2,3-Di-para-tolyl-benzo[g]quinoxaline
Rt: 3.70 min; Mol. Mass: 360
δ (ppm) = 8.79(s, 2H, 5,10-H), 8.26(m, 2H, 6,9-H), 7.65(m, 2H, 7,8-H), 7.44(d, 4H, 3',5'-H), 7.20(d, 4H, 2',6'-H, ^{3}J=8.0Hz), 2.35(s, 6H, CH_3)

(Compound 23) 2,3-Bis-(5-bromo-2-hydroxyphenyl)-benzo[g]quinoxaline
Rt: 3.69 min; Mol. Mass: 522
δ (ppm) = 10.0(b, 2H, OH), 8.81(s, 2H, 5,10-H), 8.28(m, 2H, 6,9-H), 7.68(m, 2H, 7,8-H), 7.57(s, 2H, 6'-H), 7.35(d, 2H, 4'-H), 6.68(d, 2H, 3'-H, ^{3}J=8.7Hz)

(Compound 24) 2,3-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline
Rt: 3.48 min; Mol. Mass: 392
δ (ppm) = 8.83(s, 2H, 5,10-H), 8.27(m, 2H, 6,9-H), 7.66(m, 2H, 7,8-H), 7.30(t, 2H, 5'-H, ^{3}J=7.8Hz), 7.11(s, 2H, 2'-H), 7.09(d, 2H, 6'-H), 7.00(d, 2H, 4'-H, ^{3}J=7.8Hz)

(Compound 25) 2,3-Bis-(bromomethyl)-benzo[g]quinoxaline

158 mg (1mmol) 2,3-Diaminonaphthalene was dissolved in the mixture of 1 ml DMF and 3 ml ethanol with gentle warming. After dissolving of the amine it was cooled to room temperature and the solution of 1,4-dibromo-2,3 butandione 244 mg (1mmol) in 1 ml ethanol was added with stirring. The reaction mixture was refluxed for 1 hour then allowed to cool to room temperature while the product crystallized. Crystals were collected by filtration, washed with ether and dried in vacuum.

Y: 200 mg (84%)

Rt: 3.38 min; Mol. Mass: 366

δ (ppm) = 8.79(s, 2H, 5,10-H), 8.28(m, 2H, 6,9-H), 7.68(m, 2H, 7,8-H), 5.08(s, 4H, CH_2)

(Compound 26) 2,3-Difuran-2-yl-benzo[g]quinoxaline

Rt: 3.31 min; Mol. Mass: 312.33

δ (ppm) = 8.73(s, 2H, 5,10-H), 8.22(m, 2H, 6,9-H), 7.94(d, 2H, 5'-H, ^3J=1.8Hz), 7.64(m, 2H, 7,8-H), 6.74(m, 4H, 3',4'-H)

(Compound 27) 2,3-Bis-(4-fluorophenyl)-benzo[g]quinoxaline

Rt: 3.54 min; Mol. Mass: 368.39

δ (ppm) = 8.81(s, 2H, 5,10-H), 8.26(m, 2H, 6,9-H), 7.66(m, 2H, 7,5-H), 7.58(dd, 4H, 2',6'-H, $^4J_{H,F}$=3.18Hz), 7.25(t, 4H, 3',5'-H, ^3J=8.8 Hz, $^3J_{H,F}$=11.6Hz)

(Compound 28) 2-Thiophen-3-yl-3-thiophen-2-yl-benzo[g]quinoxaline

Rt: 3.53 min; Mol. Mass:344

δ (ppm) = 8.23 (s, 2H, 5.10-H), 7.98 (m, 2H, 6.9-H), 7.95 (s, 2H, 2``-H), 7.93 (m, 2H, 5`,5``-H), 7.89 (d, 1H, 3`-H, 3j= 5.2Hz), 7.56 (m, 2H, 7.8-H), 7.30 (m, 2H, 4`,4``-H)

(Compound 29) 2,3-Bis-(thiophen-3-yl)-benzo[g]quinoxaline

Rt: 3.51 min; Mol. Mass:344

δ (ppm) = 8.20 (s, 2H, 5.10-H), 8.03 (m, 2H, 6.9-H), 7.95 (s, 2H, 2`-H), 7.88 (d, 2H, 5`-H, 3j= 4.3H_2), 7.55 (m, 2H, 7.8-H), 7.31 (d, 2H, 2`-H)

(Compound 30) 2,3-Dihydro-1H-benzo[g]cyclopenta[b]quinoxaline-1,3-dicarboxylic acid diethyl ester

Rt: 3.55 min; Mol. Mass: 364

δ (ppm) = 7.63(s, 2H, 5,10-H), 7.56(m, 2H, 6,9-H), 7.25(m, 2H, 7,8-H), 4.17(q, 4H, O-CH_2), 3.44(s, 2H, CH_2), 1.25(t, 6H, CH_3)

(Compound 31) 2-(3,4-Dimethoxyphenyl)-benzo[g]quinoxaline

100 mg (0.63 mmol) 2,3 diaminonaphthalene was dissolved in 3 ml ethanol containing 0.2 ml DMF and 126 mg (0.65 mmol) 3,4-dimethoxy phenylglyoxale was added with stirring. The reaction mixture was refluxed for 3 hours allowed to cool to room temperature and the crystals formed were filtered off, washed with ether and dried in vacuum.

Yield: 138 mg (73%)

Rt: 3.30 min; Mol. Mass: 316

δ (ppm) = 9.66(s, 2H, 2-H), 8.75(s, 2H, 5,10-H), 8.23(m, 2H, 6,9-H), 8.03(d, 1H, 6'-H), 8.00(s, 1H,), 7.18(d, 1H, 5'-H, ^3J=8.4Hz), 3.94(s, 3H, -CH_3), 3.88(s, 3H, -CH_3)

(Compound 32) 2-(3,4-Dihydroxyphenyl)-benzo[g]quinoxaline

1.67 g (10.5 mmol) 2,3-diaminonaphthalene was dissolved in 25 ml dry pyridine and 3.22 g (11 mmol) 2-chloro-2-bromo-(3',4'-dihydroxy) acetophenone was added and the mixture was refluxed in nitrogen atmosphere for 15 minutes with stirring. The crude product was filtered off after cooling and recrystallized from ethanol.

Yield: 975 mg (32%)

Rt: 3.19 min; Mol. Mass: 288

δ (ppm) = 3.66(s, 1H, OH), 9.52(s, 1H, 2-H), 9.40(s, 1H, OH), 8.71(s, 1H, 6-H), 8.68(s, 1H, 10-H), 8.22(m, 2H, 6,9-H), 7.89(s, 1H, 6-H), 7.77(d, 1H, 2'-H), 7.63(m, 2H, 7,8-H), 6.95(d, 1H, 3'-H, ^3J=6.5Hz)

(Compound 33) 2-Methyl-3-thiophen-2-yl-1,2-dihydro-benzo[g]-quinoxaline

0.949g (6 mmol) 2,3-Diamino-naphthalene, 1.314 g (6 mmol) 2-bromo-1-thiophen-2-yl-propan-1-one and 0.492 g sodiumacetate in 10 ml ethanol was refluxed for 24 hours. The solvent was removed in vacuo and the residue was purified by chromatography on silica gel. Thus 0,623g 2-methyl-3-thiophen-2-yl-1,2-dihydro-benzo[g]quinoxaline was isolated.

Rt: 3.30 min; Mol. Mass: 278.38

δ (ppm) = 8.69(s, 1H, 5-H), 8.65(s, 1H, 10-H), 7.8(m, 2H, 6,9-H), 7.24(d, 1H, 5'-H, ^3J=4.5Hz), 7.15(m, 2H, 7,8-H), 6.9(m, 2H, 3',4'-H), 4.83(q, 1H, 1-H), 1.21(d, 3H, 1-CH_3 ^3J=6.6Hz)

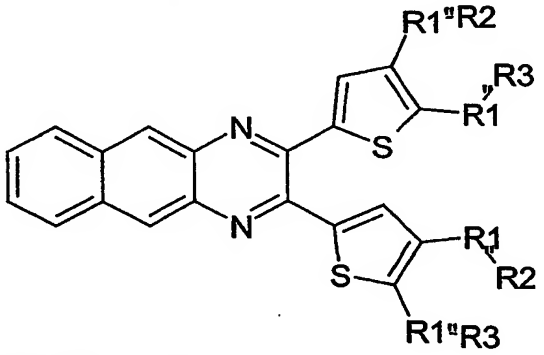
(Compound 34) 2-Methyl-3-thiophen-2-yl-benzo[g]quinoxaline

To a stirred solution of 0.278 g (1 mmol) 2-Methyl-3-thiophen-2-yl-1,2-dihydro-benzo[g]quinoxaline in 5 ml of acetone 0.158 g (1 mmol) potassium permanganate was added in portions. The stirring was continued at ambient temperature until the starting material disappeared according to TLC (eluent hexane-ethyl acetate 8:2). The manganese dioxide was collected by suction, the solvent was removed in vacuum, the residue was taken up with water, and extracted with ethyl acetate. The organic layer was separated, washed with water, dried (Na_2SO_4), filtered and evaporated to dryness. The residue was solidified under methanol. Crystals were collected by filtration and washed methanol to give 0.205 g white crystals.

Rt: 3.41 min; Mol. Mass: 276

δ (ppm) = 8.68(s, 1H, 5-H), 8.63(s, 1H, 10-H), 8.20(s, 2H, 6,9-H), 7.98(s, 1H, 5'-H), 7.89(s, 1H, 3'-H), 7.61(s, 2H, 7,8-H), 7.30(s, 1H, 4'-H), 3.32(s, 3H, $-CH_3$)

Example 8



R1=(CH2)n, n=0-6
R2 or R3 alternatively H or COOH

General Method for the synthesis of Compounds 35-38

Quinoxaline condensation was performed from the appropriate substituted methyl ω-thienyl alkylcarboxylates acid esters as given in Example 7.

(Compound 35) {5-[3-(4-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-3-yl}-acetic acid methyl ester

Rt: 3.52; Mol. Mass: 498

δ (ppm) ($CDCl_3$) = 8.61 (s, 2H, 5, 10-H), 8.07 (m, 2H, 6,9-H), 7.55 (m, 2H, 7.8-H), 7.35 (s, 2H, 5`-H), 7.33 (s, 2H, 3`-H), 3.70(s, 6H,CH_3), 3.65(s, 4H,CH_2)

(Compound 377) {5-[3-(5-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester

Rt: 3.58 ; Mol. Mass: 498

δ (ppm) ($CDCl_3$) = 8.58(s, 2H, 5, 10-H), 8.09 (m, 2H, 6,9-H), 7.56 (m, 2H, 7.8-H), 7.39 (d, 4H, ^3J=3.57Hz), 7.03 (d, 4H, 4`-H), 3.71(s, 6H, CH_3), 3.66(s, 4H, CH_2)

(Compound 37) 2,3-Bis-(2-methoxycarbonylethyl-thiophen-5-yl)-benzo[g]-quinoxaline

Rt: 3.62; Mol. Mass: 517

δ (ppm) = 8.06 (s, 2H, 5, 10-H), 7.92 (m, 2H, 6,9-H), 7.54 (m, 2H, 7.8-H), 7.35 (d, 2H, 3`-H, $^3J$=6.7 Hz), 7.73 (d, 2H, 4`-H), 4.02(s, 6H,CH_3), 2.94(t, 4H,1''-H)2.58(t,4H,2''-H)

(Compound 38) 2,3-Bis-(2-ethoxycarbonylpropyl-thiophen-5-yl)-benzo[g]-quinoxaline

79 mg (0.5 mmol) 2,3-Diaminonaphthalene was dissolved in the mixture of 1 ml DMF and 3 ml ethanol with gentle warming. After dissolving of the amine it was cooled to room temperature and the solution of 215 mg (1mmol) Compound 9 in 1 ml ethanol was added with stirring. The reaction mixture was refluxed for 1 hour then allowed to cool to room temperature while the product crystallized. Crystals were collected by filtration, washed with ether and dried in vacuum.

Yield: 200 mg (73%)

Rt: 3.92; Mol. Mass: 573

δ (ppm) = 8.63 (s, 2H, 5, 10-H), 8.19 (m, 2H, 6.9-H), 7.61 (m, 2H, 7.8-H), 7.19 (d, 2H, 4`-H, $^3J$=3.5 Hz), 6.86 (d, 2H, 3`-H)

General Method for the synthesis of Compounds 39-44

The ester function was removed as follows. 20 mg solid NaOH was dissolved in 4 ml water and added to the solution of 0.1 mmol ester in 4 ml tetrahydrofurane. The mixture was stirred for 4 hours at reflux temperature then cooled to room temperature. Its pH was adjusted to pH 3 with 1 N HCl and extracted three

times with 80 ml ethyl acetate. The organic layer dried on $CaCl_2$, and evaporated to dryness.

(Compound 39) {5-[3-(4-Carboxymethyl-thiophen-2-yl)-benzo[g]-quinoxalin-2-yl]-thiophen-3-yl}-acetic acid

Rt: 3.33; Mol. Mass: 461

δ (ppm) = 8.68(s, 2H, 5, 10-H), 8.20(m, 2H, 6, 9-H), 7.62(m, 2H, 7,8H), 7.57(s, 2H, 5-H), 7.32(s, 2H, 3-H), 3.58(s, 4H, CH_2)

(Compound 40) 2,3-Bis-(2-carboxymethyl-thiophen-5-yl)-benzo[g]-quinoxaline

Rt: ; 3.33 Mol. Mass:461

δ (ppm) = 12.72 (bs, 2H, OH), 8.68 (s, 2H, 5, 10-H), 8.20 (m, 2H, 6,9-H), 7.63 (m, 2H, 7.8-H), 7.20 (d, 2H, 3`-H, $^3J$=3.60 Hz), 6.96 (d, 2H, 4`-H), 3.94 (s, 4H, CH_2)

(Compound 41) 2,3-Bis-(2-carboxypropyl-thiophen-5-yl)-benzo[g]-quinoxaline

Rt: 3.41; Mol. Mass: 489

δ (ppm) = 11.0(bs, 2H, OH), 8.08(s, 2H, 5, 10-H), 7.98(m, 2H, 6.9-H), 7.54(m, 2H, 7.8-H), 7.35(d, 2H, 3`-H, $^3J$=6.82 $H_2$), 7.30(d, 2H, 4`-H), 2.55(m, 4H, 1``-$H_2$), 1.89(m, 4H, 2``-H_2), 2.23(m, 4H, 3``-H)

(Compound 42) 2,3-Bis-(2-carboxyethyl-thiophen-5-yl)-benzo[g]-quinoxaline

Rt: 3.41; Mol. Mass: 489

δ (ppm) = 10.75(bs, 2H, OH), 8.08(s, 2H, 5.10-H), 7.98(m, 2H, 6.9-H), 7.54(m, 2H, 7.8-H), 7.34(d, 2H, 3`-H, $^s J$=6.7 $H_2$), 7.32(d, 2H, 4`-H), 2.82(t, 4H, 1``-$H_2$), 2.56(t, 4H, 2``-H_2)

(Compound 43) {5-[5,10-Dibromo-3-(4-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-3-yl}-acetic acid

Rt: 3.91 min; Mol. Mass: 618.33

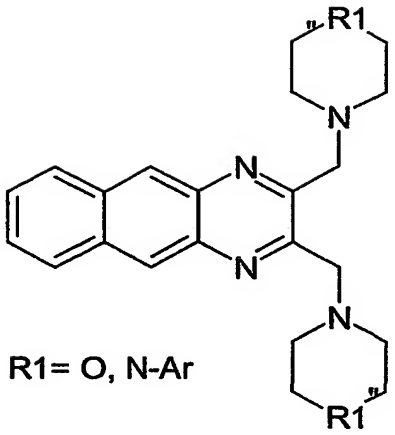
δ (ppm) = 11.0(s, 2H, OH), 8.64(m, 2H, 6,9 -H), 7.67(m, 2H, 7,8 -H), 7.50(s, 2H, 5` -H), 7.40(s, 2H, 3` -H), 3.49(s, 4H, CH_2)

(Compound 44) {5-[5,10-Dibromo-3-(5-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid

Rt: 3.84 min; Mol. Mass: 618.33

δ (ppm) = 10.8(s, 2H, OH), 7.86(m, 2H, 7,8 -H), 7.35(d, 2H, 3`-H, $^3J$ = 3.5 Hz), 7.03(d, 2H, 4`-H), 4.08(s, 2H, CH_2)

Example 9



R1= O, N-Ar

General Procedure for Compound 45-54

0.4 mmol of 2,3-bis-bromomethyl-benzo[g]quinoxaline, 0.8 mmol of secondary amine salt and 0.15 mmol of tetrabutyl ammonium bromide are weighed in a flask containing 6 ml of chloroform : 2N sodium hydroxide solution = 1 : 1 (v/v). The content of the flask is stirred or shaken for 20 – 24 hours. 20 ml of chloroform is poured to the content and the reaction mixture is extracted with 3 x 50 ml of water. The separated organic phase is dried on magnesium sulfate. After filtering the reaction mixture is evaporated to dryness in vacuum. The residue is dissolved with methanol and 1N hydrochloric acid solution, treated with charcoal, stirred for an hour and filtered. The solvent is evaporated to dryness in vacuum, and the residue is dissolved in ethanol. Diethyl ether or n-hexan is added to the solution and cooled to 0°C, and the precipitated crystals are filtered off, washed with diethyl ether or acetone, the product is dried with suction.

(Compound 45) 2,3-Bis(4-pyridin-2-yl-piperazin-1-ylmethyl)-benzo[g]-quinoxaline hydrochloride

Rt: 0.44 min; Mol. Mass: 530.68

δ (ppm) = 8.83(s, 2H, 5,10-H), 8.3 (m, 2H, 6,9-H), 8.11(d, 2H, 6'-H, ^3J = 5.5 Hz), 7.68(m, 2H, 7,8-H), 7.25 – 6.88(m, 6H, 3',4',5'-H), 5.03(s, 4H, $-CH_2$), 3.87(bs, 8H, N-CH2), 3.61(bs, 8H, N-CH_2).

(Compound 46) 2,3-Bis[4-(4-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.77 min; Mol. Mass: 564.69

δ (ppm) = 8.80(s, 2H, 5,10-H), 8.36(m, 2H, 6,9-H), 7.70(m, 2H, 7,8-H), 6.79 - 6.67(m, 8H, 2',6',3',5'-H), 5.11(s, 4H, CH_2), 3.78(bs, 8H, N-CH_2), 3.63(bs, 8H, N-CH_2).

(Compound 47) 2,3-Bis[4-(2-methoxyphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.66 min; Mol. Mass: 588.76

δ (ppm) = 8.88(s, 2H, 5,10-H), 8.35(m, 2H, 6,9-H), 7.72(m, 2H, 7,8-H), 6.95(m, 8-H, 3',4',5',6'-H), 5.18(s, 4H, CH_2), 3.88(bs, 8H, N-CH_2), 3.81(s, 6H, CH_3), 3.57(bs, 8H, N-CH_2).

(Compound 48) 2,3-Bis[4-(3-trifluoromethylphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.94 min; Mol. Mass: 664.70

δ (ppm) = 8.79(s, 2H, 5,10-H), 8.35(d, 2H, 4'-H, ^3J= 8.1 Hz), 8.28(m, 2H, 6,9-H), 7.69(m, 2H, 7,8-H), 7.65(t, 2H, 5'-H, ^3J= 6.4 Hz), 7.42(d, 2H, 6'-H), 5.01(s, 4H, CH_2), 3.70(bs, 8H, N-CH_2), 3.60(bs, 8H, N-CH_2).

(Compound 49) 2,3-Bis[4-(pyrimidin-2-yl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

146 mg (0.4 mmol) of 2,3-Bis-bromomethyl-benzo[g]quinoxaline, 190 mg (0.8 mmol) of 2,3-bis[4-(pyrimidin-2-yl)-piperazin and 0.15 mmol of tetrabutyl ammonium bromide are weighed in a flask containing 6 ml of chloroform : 2N sodium hydroxide solution = 1 : 1 (v/v). The content of the flask is stirred or shaken for 20 – 24 hours. 20 ml of chloroform is poured to the content and the reaction mixture is extracted with 3 x 50 ml of water. The separated organic phase is dried on magnesium sulfate. After filtering the reaction mixture is evaporated to dryness in vacuum. The residue is dissolved with methanol and 1N hydrochloric acid solution, treated with charcoal, stirred for an hour and filtered. The solvent is evaporated to dryness in vacuum, and the residue is dissolved in ethanol. Diethyl ether or n-hexan is added to the solution and cooled to 0°C, and the precipitated crystals are filtered off, washed with diethyl ether or acetone, the product is dried with suction.

Yield: 66 mg (31%)

Rt: 2.53 min; Mol. Mass: 532.66

δ (ppm) = 8.78(s, 2H, 5,10-H), 8.73(d, 4H, 3',5'-H, ^{3}J= 4.9 Hz), 8.30(m, 2H, 6,9-H), 7.67(m, 2H, 7,8-H), 7.42(t, 2H, 4'-H), 5.00(s, 4H, CH_2), 3.80(bs, 8H, N-CH_2), 3.56(bs, 8H, N-CH_2).

(Compound 50) 2,3-Bis[4-(3-chlorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.87 min; Mol. Mass: 597.60

δ (ppm) = 8.77(s, 2H, 5,10-H), 8.28(m, 2H, 6,9-H), 7.96(d, 2H, 4'-H, ^{3}J = 7.9 Hz), 7,41(m, 4H, 5',2'-H), 7.15(d, 2H, 6'-H, ^{3}J= 7.9 Hz), 5.02(s, 4H, CH_2), 3.78(bs, 8H, N-CH_2), 3.60(bs, 8H, N-CH_2).

(Compound 51) 2,3-Bis[4-(4-nitrophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.87 min; Mol. Mass: 597.60

δ (ppm) = 8.80(s, 2H, 5,10-H), 8.25(m, 2H, 6,9-H), 8.09(d, 4H, 3',5'-H, ^{3}J= 8.9 Hz), 6.95(d, 4H, 2',6'-H), 5.00(s, 4H, CH2), 3.88(bs, 8H, N-CH_2), 3.60(bs, 8H, N-CH_2).

(Compound 52) 2,3-Bis[4-(2-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

Rt: 2.76 min; Mol. Mass: 564.69

δ (ppm) = 11.56; 9.35(s, 1H, HCl), 8.88(s, 2H, 5,10-H), 8.28(m, 2H, 6,9-H), 7.72(m, 2H, 7,8-H), 7.21 – 6.98(m, 8H, 3',4',5',6'-H), 4.92(s, 4H, CH_2), 3.20(s, 16 H, N-CH_2).

(Compound 53) 2,3-Bis-piperidin-1-ylmethyl-benzo[g]quinoxaline hydrochloride

Rt: 0.38 min; Mol. Mass: 374.53

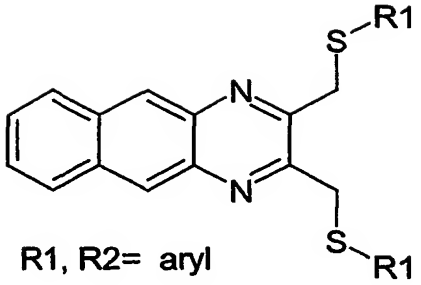
δ (ppm) = 10.81(s, 2H, HCl), 8.87(s, 2H, 5,10-H), 8.36(m, 2H, 6,9-H), 7.74(m, 2H, 7,8-H), 4.97(s, 4H, CH_2), 2.75; 2.15; 1.55(m, 20H, piperidine).

(Compound 54) 2,3-Bis-morpholin-4-ylmethyl-benzo[g]quinoxaline hydrochloride

Rt: 0.39 min; Mol. Mass: 378.48

δ (ppm) = 9.72(s, 2H, HCl), 8.86(s, 2H, 5,10-H), 8.35(m, 2H, 6,9-H), 7.73(m, 2H, 7,8-H), 5.12(s, 4H, CH_2), 3.74(s, 8H, O-CH_2), 2.51(s, 8H, N-CH_2).

Example 10



R1, R2= aryl

General Method for the synthesis of Compounds 55-74

146 mg (0.4 mmol) 2,3-Bis-bromomethyl-benzo[g]quinoxaline, (0.8 mmol) substituted-benzenethiol, 50 mg (0.15 mmol) tetrabutylammonium bromide, 5 ml of chloroform and 3 ml 2N aqueous sodium hydroxide solution were stirring vigorously under argon at ambient temperature for 24 hours. The organic layer was separated, washed with water, dried (Na_2SO_4), filtered and evaporated to dryness. The residue was solidified under methanol. Crystals were collected by filtration and washed methanol to give the named product.

(Compound 55) 2,3-Bis-(phenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.68 min; Mol. Mass: 424

δ (ppm) = 8.50(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 7.39(m, 4H, 2',6'-H, ^3J=8.0Hz), 7.21(m, 6H, 3',4',5'-H), 4.55(s, 4H, CH_2)

(Compound 56) 2,3-Bis-(4-methylphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.83 min; Mol. Mass: 452

δ (ppm) = 8.49(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 7.26(d, 4H, 2',6'-H, ^3J=8.0Hz), 7.03(d, 4H, 3',5'-H), 4.55(s, 4H, CH_2), 2.88(s, 6H, CH_3)

(Compound 57) 2,3-Bis-(2-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.58 min; Mol. Mass: 484

δ (ppm) = 8.43(s, 2H, 5,10-H), 8.04(m, 2H, 6,9-H), 7.53(m, 2H, 7,8-H), 7.47(d, 2H, 6'-H, ^3J=8.1Hz), 7.21(t, 2H, 4'-H), 6.83(t, 2H, 5'-H), 6.74(d, 2H, 3'-H, ^3J=8.1Hz), 4.63(s, 4H, CH_2), 3.63(s, 6H, CH_3)

(Compound 58) 2,3-Bis-(4-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.61 min; Mol. Mass: 484

δ (ppm) = 8.45(s, 2H, 5,10-H), 8.05(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 7.26(m, 4H, 2',6'-H, ^{3}J=8.4Hz), 6.71(d, 4H, 3',5'-H), 4.47(s, 4H, CH_2), 3.72(s, 6H, CH_3)

(Compound 59) 2,3-Bis-(2,5-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 4.33 min; Mol. Mass: 562

δ (ppm) = 8.56(s, 2H, 5,10-H), 8.09(m, 2H, 6,9-H), 7.77(d, 2H, 6'-H ^{4}j=2.2Hz), 7.58(m, 2H, 7,8-H), 7.24(d, 2H, 3'-H, ^{3}J=8.6Hz), 7.08(dd, 2H, 4'-H), 4.73(s, 4H, CH_2)

(Compound 60) 2,3-Bis-(2,6-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.93 min; Mol. Mass: 562

δ (ppm) = 8.27(s, 2H, 5,10-H), 8.00(m, 2H, 6,9-H), 7.52(m, 2H, 7,8-H), 7.23(m, 4H, 3',5'-H), 7.10(m, 2H, 4'-H), 4.66(s, 4H, CH_2)

(Compound 61) 2,3-Bis-(3,4-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 4.39 min; Mol. Mass: 562

δ (ppm) = 8.53(s, 2H, 5,10-H), 8.09(m, 2H, 6,9-H), 7.58(m, 4H, 7,8,2'-H), 7.23(m, 4H, 5',6'-H), 4.64(s, 4H, CH_2)

(Compound 62) 2,3-Bis-(2,4-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 4.05 min; Mol. Mass:480

δ (ppm) = 8.48(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 7.26(d, 2H, 6'-H, ^{3}J=7.8Hz), 6.96(s, 2H, 3'-H), 6.87(s, 2H, 5'-H), 4.47(s, 4H, CH_2), 2.28(s, 6H, CH_3), 2.25(s, 6H, CH_3)

(Compound 63) 2,3-Bis-(2,5-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 4.04 min; Mol. Mass: 480

δ (ppm) = 8.50(s, 2H, 5,10-H), 8.07(m, 2H, 6,9-H), 7.56(m, 2H, 7,8-H), 7.23(s, 2H, 6'-H), 7.02(d, 4H, 3',4'-H, ^{3}J=7.7Hz), 4.55(s, 4H, CH_2), 2.31(s, 6H, CH_3), 2.19(s, 6H, CH_3)

(Compound 64) 2,3-Bis-(2,3,5,6-tetrafluorophenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.67 min; Mol. Mass: 568

δ (ppm) = 8.40(s, 2H, 5,10-H), 8.05(m, 2H, 6,9-H), 7.57(m, 2H, 7,8-H), 7.01(m, 2H, 4'-H), 4.65(s, 4H, CH_2)

(Compound 65) 2,3-Bis-(2-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.86 min; Mol. Mass: 493
δ (ppm) = 8.50(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.57(m, 6H, 7,8,3'-H), 7.34(m, 2H, 6'-H), 7.15(m, 4H, 4',5'-H), 4.71(s, 4H, CH_2)

(Compound 66) 2,3-Bis-(3-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.97 min; Mol. Mass: 493
δ (ppm) = 8.53(s, 2H, 5,10-H), 8.08(m, 2H, 6,9-H), 7.57(m, 2H, 7,8-H), 7.26(m, 2H, 2'-H), 7.15(m, 6H, 4',5',6'-H), 4.66(s, 4H, CH_2)

(Compound 67) 2,3-Bis-(4-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.94 min; Mol. Mass: 493
δ (ppm) = 8.50(s, 2H, 5,10-H), 8.07(m, 2H, 6,9-H), 7.57(m, 2H, 7,8-H), 7.32(d, 4H, 2',6'-H, ^3J=8.5Hz), 7.21(d, 4H, 3',5'-H), 4.60(s, 4H, CH_2)

(Compound 68) 2,3-Bis-(2-bromophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.93 min; Mol. Mass: 582
δ (ppm) = 8.50(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.56(m, 6H, 7,8,3',6'-H), 7.26-7.04(m, 4H, 4',5'-H), 4.72(s, 4H, CH_2)

(Compound 69) 2,3-Bis-(3-bromophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 4.07 min; Mol. Mass: 582
δ (ppm) = 8.53(s, 2H, 5,10-H), 8.08(m, 2H, 6,9-H), 7.64(s, 2H, 2'-H), 7.56(m, 2H, 7,8-H), 7.29(m, 4H, 4',6'-H), 7.10(m, 2H, 5'-H), 4.65(s, 4H, CH_2)

(Compound 70) 2,3-Bis-(4-fluorophenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.67 min; Mol. Mass: 460
δ (ppm) = 8.45(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.56(m, 2H, 7,8-H), 7.34(m, 4H, 2',6'-Hz), 6.91(m, 4H, 3',5'-H), 4.55(s, 4H, CH_2)

(Compound 71) 2,3-Bis-(2-methylphenylsulfanylmethyl)-benzo[g]quinoxaline
Rt: 3.83 min; Mol. Mass: 452
δ (ppm) = 8.49(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 7.41(d, 2H, 3'-H, ^3J=8.2Hz), 7.10(m, 6H, 4',5',6'-H), 4.56(s, 4H, CH_2), 2.33(s, 6H, CH_3)

(Compound 72) 2,3-Bis-(3-methylphenylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.86 min; Mol. Mass: 452

δ (ppm) = 8.50(s, 2H, 5,10-H), 8.06(m, 2H, 6,9-H), 7.57(m, 2H, 7,8-H), 7.20 - 6.98(m, 8H, 2',4',5',6'-H), 4.62(s, 4H, CH_2), 2.23(s, 6H, CH_3)

(Compound 73) 2,3-Bis-(4,5-dihydro-thiazol-2-yl-sulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.51 min; Mol. Mass: 442

δ (ppm) = 8.72(s, 2H, 5,10-H), 8.24(m, 2H, 6,9-H), 7.66(m, 2H, 7,8-H), 4.97(s, 4H, CH_2), 4.18(t, 4H, 5'-H, ^3J=8.02Hz), 3.50(t, 4H, 4'-H)

(Compound 74) 2,3-Bis-(1H-benzoimidazol-2-ylsulfanylmethyl)-benzo[g]quinoxaline

Rt: 3.12; Mol. Mass. 504.64

δ (ppm) = 8.77(s, 2H, 5,10-H), 8.25(m, 3H, 6,9-H), 7.90(d, 2H, 5'-H, ^3J =7.8Hz), 7.67(m, 3H, 7,8-H, NH), 7.47(d, 2H, 8'-H, ^3J=7.3Hz), 7.31-7.17(m, 4H, 6',7'-H), 5.96(s, 2H, S-CH_2), 5.05(s, 2H, S-CH_2)

Example 11

(Compound 75) (3-Methoxycarbonylmethylsulfanylmethyl-benzo[g]-quinoxalin-2-ylmethylsulfanyl)-acetic acid methyl ester

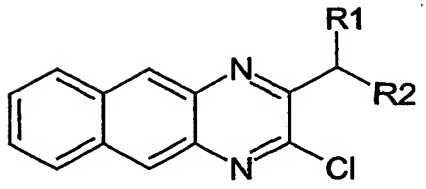
183 mg (0.5 mmol) 2,3-Bis-bromomethyl-benzo[g]quinoxaline, 127 mg (1.2 mmol) methyl thioglycolate and 141 mg (1.4 mmol) triethylamine in 2 ml of THF were stirred under argon at ambient temperature over 4 hours. The solvent was evaporated under reduced pressure. The residue was solidified under diethylether. Crystals were collected by filtration, washed with ether, methanol, water, and methanol.

Yield: 94 mg, (45%)

Rt: 3.15 min.; Mol. Mass. 416

δ (ppm) = 8.67(s, 2H, 5,10-H), 8.23(m, 2H, 6,9-H), 7.86(m, 2H, 7,8-H), 4.32(s, 4H, 3'H_2), 3.52(s, 4H, 1'-H_2), 3.43(s, 6H, -CH_3)

Example 12



R1, R2= CN, COOR, CONHR

General Method for the synthesis of Compounds 76-80

125 mg (0.5 mmol) 2,3-Dichlorobenzo[g]quinoxaline and (0.5 mmol) active methylene compound were dissolved in 1 ml dioxane and 50 mg NaH was added. This mixture was refluxed for 20 minutes to two hours and the precipitated product was filtered off from the hot reaction mixture and washed with hexane.

(Compound 76) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malononitrile

2.5 g 2,3-Dichlorobenzo[g]quinoxaline and 0.75 g malononitrile were dissolved in 20 ml dioxane and 0.5 g NaH was added. This mixture was refluxed for 1 hour and the precipitated product was filtered off from the hot reaction mixture and washed with hexane and with 1 N aqueous solution of HCl and dried.

Yield: 2.3 g (82%)

Rt: 4.57 min; Mol. Mass: 278

δ (ppm) = 8.21(s, 1H, 5-H), 8.00(s, 1H, 10-H), 7.96(m, 2H, 6,9-H), 7.41(m, 2H, 7,8-H)

(Compound 77) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malonic acid diethyl ester

Rt: 3.35 min; Mol. Mass: 372

δ (ppm) = 8.53(s, 1H, 5-H), 8.51(s, 1H, 10-H), 8.17(m, 2H, 6,9-H), 7.60(m, 2H, 7,8-H), 3.86(q, 4H, CH_2), 3.33(s, 1H, CH), 0.98(t, 6H, CH_3)

(Compound 78) (3-Chloro-benzo[g]quinoxalin-2-yl)-cyano-acetic acid ethyl ester

Rt: 3.33 min; Mol. Mass: 325

δ (ppm) = 8.33(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.05(m, 2H, 6,9-H), 7.49(m, 2H, 7,8-H), 3.99(q, 2H, CH_2), 3.33(s, 1H, CH), 1.17(t, 3H, CH_3)

(Compound 79) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-2-cyano-N-(4-trifluoromethyl-phenyl)-acetamide

Rt:3.65 ; Mol. Mass:440

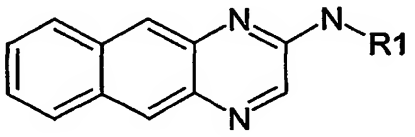
δ (ppm) = 8.20(s, 2H, 5,10-H), 8.02-7.88(m, 6H, 6,9,2',3',5',6'-H), 7.39(m, 2H, 7,8-H), 3.56(s, 1H, CH)

(Compound 80) N-(3,5-Bis-trifluoromethyl-phenyl)-2-(3-chloro-benzo[g]quinoxalin-2-yl)-2-cyano-acetamide

Rt: 3.89 ;Mol. Mass: 508

δ (ppm) = 8.58(s, 2H, 5,10-H), 8.22, 8.20(s, 2H, 2',6'-H), 8.03(m, 3H, 6,9,4'-H), 7.42(m, 2H, 7,8-H), 3.56(s, 1H, CH)

Example 13



R1= aryl

General Method for the synthesis of Compounds 81-99

107 mg (0.5 mmol) 2-chloro benzo[g]quinoxaline was dissolved in the mixture of 3 ml 2-propanol and 0.2 ml N,N-dimethylformamide (DMF). 0.55 mmol amine or hydrazine compound and 0.07 ml (0.5 mmol) triethylamine were added. The reaction mixture was stirred at room temperature for three hours then evaporated to dryness in vacuum. The residue was crystallized from ethanol-water.

(Compound 81) Benzo[g]quinoxalin-2-yl-(2-ethoxycarbonylphenyl)-amine

Rt: 3.65 min; Mol. Mass: 343

δ (ppm) = 10.09(s, 1H, NH), 8.70(s, 1H, 5-H), 8.54(s, 1H, 2-H), 8.39(s, 1H, 10-H), 8.11(m, 2H, 6,9-H), 8.01(d, 2H, 3'-H, ^3J=7.8Hz), 7.73(m, 1H, 5'-H), 7.53(m, 3H, 7,8,6'-H), 7.21(m, 1H, 4'-H), 4.29(q, 2H, CH_2), 1.28(t, 3H, CH_3)

(Compound 82) 4-(Benzo[g]quinoxalin-2-ylamino)-benzenesulfonamide

Rt: 3.11 min; Mol. Mass: 350

δ (ppm) = 10.59(s, 1H, NH), 8.73(s, 1H, 2-H), 8.53(s, 1H, 5-H), 8.36(s, 1H, 10-H), 8.25(d, 2H, 3',5'-H, ^{3}J=8.8Hz), 8.13(m, 2H, 6,9-H), 7.86(d, 2H, 2',6'-H), 7.54(m, 2H, 7,8-H), 7.28(ts, 2H, NH_2)

(Compound 83) Benzo[g]quinoxalin-2-yl-(3,4-dimethylphenyl)-amine

Rt: 3.53 min; Mol. Mass: 299

δ (ppm) = 10.37(s, 1H, NH), 8.69(s, 1H, 2-H), 8.48(s, 1H, 5-H), 8.24(s, 1H, 10-H), 7.82(d, 1H, 6'-H, ^{3}J=8.1Hz), 7.75(s, 1H, 2'-H), 7.52(m, 2H, 7,8-H), 7.19(d, 1H, 5'-H), 2.29(s, 3H, CH_3), 2.23(s, 3H, CH_3)

(Compound 84) Benzo[g]quinoxalin-2-yl-[3,5-bis-(ethoxycarbonyl)-phenyl] amine

Rt: 3.46 min; Mol. Mass: 387

δ (ppm) = 10.70(s, 1H, NH), 9.01(s, 2H, 4'-H), 8.68(s, 1H, 5-H), 8.55(s, 1H, 10-H), 8.25(s, 1H, 2'-H), 8.14(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H), 3.96(s, 6H, CH_3)

(Compound 85) Benzo[g]quinoxalin-2-yl-(2-hydroxy-4-methylphenyl)-amine

Rt: 3.33 min; Mol. Mass: 301

δ (ppm) = 10.05(b, 1H, H), 8.91(s, 1H, 2-H), 8.54(s, 1H, 5-H), 8.20(s, 1H, 10-H), 8.04(m, 2H, 6,9-H), 7.92(d, 1H, 6'-H), 7.90(bs, 1H, OH), 7.55(m, 2H, 7,8-H), 6.86(s, 1H, 3'-H), 6.75(d, 1H, 5'-H, ^{3}J=8.1 Hz), 2.29(s, 1H, CH_3)

(Compound 86) Benzo[g]quinoxaline-2-yl-phenylamine

The compound was obtained from 100 mg (0.63 mM) 2-chloro-benzo[g]quinoxaline dissolved in the mixture of 3 ml ethanol and 1 ml DMF. 120 µl aniline and 3 drops of methanol saturated with HCl were added and stirred at 50°C for one hour. The solvent was removed in vacuum and the residue was triturated with 50% aqueous ethanol and filtered.

Yield: 131 mg (77%)

Rt: 3.51 min; Mol. Mass: 271

δ (ppm) = 10.11(s, 1H, NH), 8.56(s, 1H, 6, 2-H), 8.48(s, 1H, 5-H), 8.27(s, 1H, 10-H), 8.08(m, 4H, 6,9,2'6'-H), 7,48(m, 4H, 7,8,3'5'-H), 7.07(t, 1H, ^{3}J=7.2Hz)

(Compound 87) Benzo[g]quinoxalin-2-yl-biphenyl-4-yl-amine

Rt: 3.70 min; Mol. Mass: 347

δ (ppm) = 10.35(s, 1H, NH), 8.70(s, 1H, 2-H), 8.50(s, 1H, 5-H), 8.30(s, 1H, 10-H), 8.20(d, 2H, 3',5'-H, ^{3}J=8.7Hz), 8.11(m, 2H, 6,9-H), 7.72(m, 4H, 2',6',2'',6''-H), 7.59-7.32(m, 5H, 7,8,3'',4'',5''-H)

(Compound 88) Benzo[g]quinoxalin-2-yl-(4-methylphenyl)-amine
Rt: 3.46 min; Mol. Mass: 285
δ (ppm) = 10.20(s, 1H, NH), 8.66(s, 1H, 2-H), 8.47(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.09(m, 2H, 6,9-H), 7.95(d, 2H, 3',5'-H, ^{3}J=8.3Hz), 7.52(m, 2H, 7,8-H), 7.23(d, 2H, 2',6'-H)

(Compound 89) Benzo[g]quinoxalin-2-yl-(4-phenoxyphenyl)-amine
Rt: 3.65 min; Mol. Mass: 363
δ (ppm) = 10.40(s, 1H, NH), 8.69(s, 1H, 2-H), 8.49(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.09(m, 4H, 6,9,3',5'-H), 7.57-7.37(m, 4H, 7,8,3'',5''-H), 7.14-7.00(m, 7H, 2',6',2'',6'',4''-H)

(Compound 90) Benzo[g]quinoxalin-2-yl-(4-bromophenyl)-amine
Rt: 3.64 min; Mol. Mass: 350
δ (ppm) = 10.42(s, 1H, NH), 8.69(s, 1H, 2-H), 8.50(s, 1H, 5-H), 8.28(s, 1H, 10-H), 8.10(m, 4H, 6,9,3',5'-H), 7.59(d, 2H, 2',6'-H, ^{3}J=8.9Hz), 7.52(m, 2H, 7,8-H)

(Compound 91) Benzo[g]quinoxalin-2-yl-(4-methylsulfanylphenyl)-amine
Rt: 3.52 min; Mol. Mass: 312
δ (ppm) = 10.34(s, 1H, NH), 8.67(s, 1H, 2-H), 8.48(s, 1H, 5-H), 8.12(s, 1H, 10-H), 8.07(m, 1H, 6,9,3'5'-H) 7.52(m, 2H, 7,8-H), 7.35(d, 2H, 2',6'-H, ^{3}J=8.6Hz)

(Compound 92) [4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-phenylmethanone
Rt: 3.61 min; Mol. Mass: 375
δ (ppm) = 10.65(s, 1H, NH), 8.75(s, 1H, 2-H), 8.54(s, 1H, 5-H), 8.36(s, 1H, 10-H), 8.28(d, 2H, 3',5'-H, ^{3}J=8.7Hz) 8.13(m, 2H, 6,9-H), 7.86(d, 2H, 2',6'-H), 7.77-7.50(m, 5H, 2'',3'',4'',5'',6''-H)

(Compound 93) Benzo[g]quinoxalin-2-yl-(2,4-dimethoxyphenyl)-amine
Rt: 3.29 min; Mol. Mass: 331

δ (ppm) = 12.00(b, 1H, NH), 8.89(s, 1H, 2-H), 8.53(s, 1H, 5-H), 8.18(s, 1H, 10-H), 8.09(m, 3H, 6,9,6'-H) 7.54(m, 2H, 7,8-H), 6.77(d, 1H, 3'-H, 4J=2.3Hz), 6.67(dd, 1H, 5'-H)

(Compound 94) Benzo[g]quinoxalin-2-yl-(2-hydroxy-5-chlorophenyl)-amine

Rt: 3.50 min; Mol. Mass: 322

δ (ppm) = 9.51(bs, 1H, OH), 9.00(s, 1H, 2-H), 8.82(s, 1H, 6'-H), 8.51(s, 1H, 5-H), 8.26(s, 1H, 10-H), 8.12(m, 2H, 6.9-H), 7.54(m, 2H, 7.8-H), 6.99(m, 2H, 3'4'-H)

(Compound 95) Benzo[g]quinoxalin-2-yl-(3-fluoro-4-methylphenyl)-amine

Rt: 3.56 min; Mol. Mass: 303

δ (ppm) = 10.36(s, 1H, NH), 8.66(s, 1H, 2-H), 8.50(s, 1H, 5-H), 8.30(s, 1H, 10-H), 8.21(d, 1H, 6'-H, ^{3}J=12.72 H_2), 8.10(m, 2H, 6.9-H), 7.54(m, 3H, 7,8,2'-H), 7.28(m, 1H, 3'-H)

(Compound 96) Benzo[g]quinoxalin-2-yl-[2-(2-chlorophenyl)-ethyl]-amine

Rt: 3.27 min; Mol. Mass: 334

δ (ppm) = 8.38(s, 2H, 2.5-H), 8.28(m, 1H, NH), 8.06(s, 1H, 10-H), 7.99(m, 2H, 6.9-H), 7.52-7.25(m, 6H, 7,8,3',4',5',6'-H), 3.70(m, 2H, a-H_2), 3.11(t, 2H, b-H_2,^{3}J=7.4H_2)

(Compound 97) Benzo[g]quinoxalin-2-yl-(3-bromophenyl)-amine

Rt: 3.66 ;Mol. Mass: 350

δ (ppm) = 10.5(s, 1H, NH), 8.71(s, 1H, 2-H), 8.52(s, 2H, 5,10-H), 8.29(s, 1H, 2'-H), 8.12(m, 2H, 6,9-H), 7.97(d, 1H, 4'-H, ^{3}J=8.2Hz), 7.54(m, 2H, 7,8-H) 7.37(t, 1H, 5'-H), 7.25(d, 1H, ^{3}J=7.9Hz)

(Compound 98) Benzo[g]quinoxaline-2-yl-(3,4-dimethoxyphenyl)-amine

300 mg (1.42 mmol) 2-chloro-benzo[g]quinoxaline was refluxed in abs. ethanol with 220 mg (1.44 mmol) 3,4-dimethoxy aniline. After cooling the product crystallized and was isolated by filtration. The crude material was recrystallized from isopropyl alcohol.

Yield: 343mg (73%)

δ (ppm) = 9.11(s, 1H, NH), 8.83(s, 1H, 2-H), 8.50(d, 1H, 5'-H, ^{3}J=8.8Hz), 8.43(s, 1H, 5-H), 8.13(s, 1H, 10-H), 8.04(m, 2H, 6,9-H), 7.48(m, 2H, 7,8-H), 6.71(d, 1H, 2"-H, ^{4}J=2.4Hz), 6.62(dd, 1H, 6'-H), 3.89(s, 3H, -CH_3), 3.80(s, 3H, CH_3)

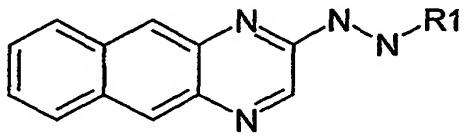
(Compound 99) 4-(Benzo[g]quinoxaline-2-yl-amino)-benzene-1,2-diol

400 mg (1.3 mmol) 2-(3,4-dimethoxyphenyl)-amino-benzo[g]quinoxaline was refluxed in 20 ml dry benzene with 0.69 g (4 x equivalent) aluminium chloride. The mixture was boiled until all the methyl chloride formed in the reaction steamed off. The mixture was evaporated to dryness, the resulting tar compound was dissolved in ethanol and decolorized by charcoal. The product was further purified by dissolving it in 2 M hydrochloric acid and after filtration precipitated with sodium carbonate solution, filtrated and dried in vacuum.

Yield:250 mg (64%)

δ (ppm) = 9.23(bs, 1H, NH), 9.04(bs, 2H, OH), 8.83(s, 1H, 2-H), 8.49(d, 1H, 5'-H, ^{3}J=8.8Hz), 8.43(s, 1H, 5-H), 8.15(s, 1H, 10-H), 8.03(m, 2H, 6,9-H), 7.49(m, 2H, 7,8-H), 6.71(d, 1H, 2"-H4 J=2.4Hz), 6.60(dd, 1H, 6'-H)

Example 14



R1= aryl

General procedure for compounds 100 – 103 are according to the reaction protocol for compounds 81 – 99.

(Compound 100) N-Benzo[g]quinoxalin-2-yl-N'-(4-fluorophenyl)-hydrazine

Rt: 3.25 min; Mol. Mass: 304

δ (ppm) = 10.13(s, 2H, NH), 8.70(s, 1H, 2-H), 8.48(s, 1H, 5-H), 8.23(s, 1H, 10-H), 8.03(m, 2H, 6,9-H), 7.52(m, 2H, 7,8-H), 7.19-7.06(m, 4H, 2',3',5',6'-H)

(Compound 101) N-Benzo[g]quinoxalin-2-yl-N'-(2,4-dichlorophenyl)-hydrazine

107 mg (0.5 mmol) 2-Chlorobenzo[g]quinoxaline was dissolved in the mixture of 3 ml 2-propanol and 0.2 ml DMF. 40 mg (0.55 mmol) 2,4-Dichlorophenyl hydrazine and 0.07 ml (0.5 mmol) triethylamine were added. The reaction mixture was stirred at room temperature for three hours then evaporated to dryness in vacuum. The residue was crystallized from ethanol-water.

Yield: 86 mg (61%)
Rt: 3.61 min; Mol. Mass: 355
δ (ppm) = 8.52(bs, 1H, NH), 8.31(s, 1H, 5-H), 8.24(s, 1H, 10-H), 7.90(m, 2H, 6.9-H), 7.66(bs, 1H, NH), 7.58-7.24(m, 5H, 7,8,3',5',6'-H)

(Compound 102) N-Benzo[g]quinoxalin-2-yl-N'-(3-chlorophenyl)-hydrazine
Rt: 3.48 min; Mol. Mass: 321
δ (ppm) = 9.90(b, 1H, NH), 8.22(s, 1H, 5-H), 8.13(s, 1H, 10-H), 7.89(m, 2H, 6,9-H), 7.64(bs, 1H, NH), 7.46(m, 2H, 7,8-H), 7.28-7.19(m, 2H, 2',5'-H), 7.06(d, 1H, 4'-H, ^{3}J=8.1Hz), 6.82(d, 1H, 6'-H, ^{3}J=7.7Hz)

(Compound 103) N-Benzo[g]quinoxalin-2-yl-N'-(4-chlorophenyl)-hydrazine
Rt: 3.44 min; Mol. Mass: 321
δ (ppm) = 9.80(b, 1H, NH), 8.18(s, 1H, 5-H), 8.10(s, 1H, 10-H), 7.88(m, 2H, 6,9-H), 7.60(bs, 1H, NH), 7.44(m, 2H, 7,8-H), 7.28(d, 2H, 3',5'-H, ^{3}J=8.8Hz), 7.14(d, 2H, 6',2'-H)

Example 15

(Compound 104) 1-(2-Nitrophenyl)-2-(3-thiophen-2-yl-benzo[g]quinoxaline-2-yl)-ethanol

110 mg (0.4 mmol) 2-Methyl-3-thiophen-2-yl-benzo[g]quinoxaline and 76 mg (0.4 mmol) 2-nitrobenzaldehyde was refluxed in 2 ml acetic anhydride for 4 hours. The solvent was evaporated under reduced pressure. The residue was solidified under methanol. Crystals were collected by filtration, washed with water and methanol.
Yield: 39mg
Rt: 3.63 min; Mol. Mass: 427.49
δ (ppm) = 8.70(s, 1H, 5-H), 8.65(s, 1H, 10-H), 8.23(m, 3H, 6,9,3"-H), 7.99-7.82(m, 4H, 3',4',5',6'-H), 7.62(m, 3H, 7,8,5"-H), 7.28(m, 2H, 3",4"-H), 6.01(m, 1H, ethyl-1-H), 5.82(d, 1H, OH, ^{3}J=4.5Hz), 3.76(m, 2H, ethyl-2-H)

Example 16

General Method for the synthesis of Compounds 105-116

107 mg (0.5 mmol) 2-chloro benzo[g]quinoxaline was dissolved in the mixture of 2 ml 2-propanol and 3 ml DMF. 0.55 mmol amine and 0.6 ml methanol

saturated with HCl was added. The reaction mixture was stirred at 50°C for two hours then evaporated to dryness in vacuum. The residue was crystallized from ethanol-water.

(Compound 105) Benzo[g]quinoxalin-2-yl-(4-ethylphenyl)-amine
Rt: 3.58 min; Mol. Mass: 299
δ (ppm) = 10.30(s, 1H, NH), 8.68(s, 1H, 2-H), 8.48(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.09(m, 2H, 6.9-H), 7.97(d, 2H, 3',5'-H, ^3J=8.6H_2), 7.53(m, 2H, 2.8-H), 7.27(d, 2H, 2',6'-H), 2.61(m, 2H, CH_2), 1.21(t, 3H, CH_2,^3J=4.6H_2)

(Compound 106) N-[4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide
Rt: 3.14 min; Mol. Mass: 328
δ (ppm) = 10.27(bs, 1H, NH), 9.98(s, 1H, NH), 8.65(s, 1H, 3-H), 8.47(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.08(m, 2H,6.9-H), 7.99(d, 2H, 3',5'-H, ^3J=8.9H_2), 7.63(d, 2H, 2',6'-H), 7.50(m, 2H, 7.8-H), 2.06(s, 3H, -CH_3)

(Compound 107) Benzo[g]quinoxalin-2-yl-(3-chlorophenyl)-amine
Rt: 3.60 min; Mol. Mass: 306
δ (ppm) = 10.47(s, 1H, NH), 8.68(s, 1H, 3-H), 8.48(s, 1H, 5-H), 8.40(s, 1H, 10-H), 8.28(s, 1H, 2'-H), 8.01(m, 2H,6.9-H), 7.88(d, 1H, 4'-H, ^3J=8.2H_2), 7.51(m, 2H, 7,8-H), 7.41(t, 1H, 5'-H), 7.10(d, 1H,6'-H)

(Compound 108) Benzo[g]quinoxalin-2-yl-(4-chlorophenyl)-amine
Rt: 3.58 min; Mol. Mass: 306
δ (ppm) = 10.47(bs, 1H, NH), 8.69(s, 1H, 3-H), 8.48(s, 1H, 5-H), 8.26(s, 1H, 10-H), 8.11(d, 2H, 3',5'-H, ^3J=8.9H_2), 8.09(m, 2H,6.9-H), 7.52(m, 2H, 7,8-H), 7.44(d, 2H, 2',6'-H)

(Compound 109) Benzo[g]quinoxalin-2-yl-(3-fluorophenyl)-amine
Rt: 3.45 min; Mol. Mass: 289
δ (ppm) = 10.48(s, 1H, NH), 8.69(s, 1H, 3-H), 8.51(s, 1H, 5-H), 8.33(s, 1H, 10-H), 8.28(m, 1H, 2'-H,), 8.12(m, 2H,6.9-H), 7.68-7.39(m, 4H, 7,8,4',6'-H), 6.89(m, 1H, 5'-H)

(Compound 110) Benzo[g]quinoxalin-2-yl-(2-fluorophenyl)-amine
Rt: 3.34 min; Mol. Mass: 389

δ (ppm) = 9.78(s, 1H, NH), 8.88(s, 1H, 3-H), 8.72(m, 1H, 5'-H), 8.50(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.51(m, 2H, 7,8-H), 7.35-7.12(m, 3H, 3',4',6'-H)

(Compound 111) Benzo[g]quinoxalin-2-yl-(2,4-dichlorophenyl)-amine
Rt: 3.66 min; Mol. Mass: 340
δ (ppm) = 9.7(b, 1H, NH), 8.94(s, 1H, 2-H), 8.53(s, 1H, 5-H), 8.47(d, 1H, 5'-H, $^3J=8.8H_2$), 8.20(s, 1H, 10-H), 8.09(m, 2H, 6.9-H), 7.73(d, 1H, 3'-H, $^4J=2.1H_2$), 7.58-7.47(m, 3H, 7,8,6'-H)

(Compound 112) Benzo[g]quinoxalin-2-yl-(4-hydroxyphenyl)-amine
Rt: 3.17 min; Mol. Mass: 287
δ (ppm) = 10.70(s, 1H, NH), 8.69(s, 1H, 3-H), 8.49(s, 1H, 5-H), 8.19(s, 1H, 10-H), 8.07(m, 2H, 6,9-H), 7.74(d, 2H, 3',5'-H, $^3J=8.7H_2$), 7.53(m, 2H, 7,8-H), 6.87(d, 2H, 2',6'-H)

(Compound 113) Benzo[g]quinoxalin-2-yl-(3-iodophenyl)-amine
Rt: 3.73 min; Mol. Mass: 397
δ (ppm) = 10.42(s, 1H, NH), 8.69(s, 1H, 3-H), 8.61(s, 1H, 2'-H), 8.51(s, 1H, 5-H), 8.27(s, 1H, 10-H), 8.13(m, 2H, 6,9-H), 8.05(d, 1H, 2'-H, $^3J=8.2H_2$), 7.52(m, 2H, 7,8-H), 7.43(d, 1H, 4'-H, $^3J=8.2H_2$), 7.21(t, 1H, 5'-H)

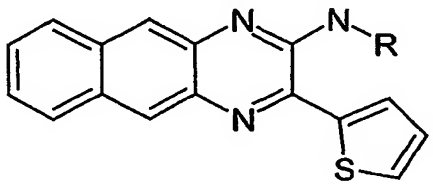
(Compound 114) Benzo[g]quinoxalin-2-yl-(3,4-dichlorophenyl)-amine
Rt: 3.86 min; Mol. Mass: 340
δ (ppm) = 10.61(bs, 1H, NH), 8.82(s, 2H, 3,5-H), 8.70(s, 1H, 10-H), 8.12(m, 3H, 6,9,5'-H), 7.57(4H, 7,8,2',6'-H)

(Compound 115) Benzo[g]quinoxalin-2-yl-(3-trifluoromethylphenyl)-amine
Rt: 3.63 min; Mol. Mass: 339
δ (ppm) = 10.47(s, 1H, NH), 8.66(s, 1H, 3-H), 8.63(s, 1H, 5-H), 8.53(s, 1H, 10-H), 8.28(s, 1H, 2'-H), 8.64(d, 1H, 4'-H, $^3J=7.9H_2$), 8.13(m, 2H, 6,9-H), 7.58(m, 3H, 7,8,5'-H), 7.41(d, 1H, 6'-H, $^3J=7.9H_2$)

(Compound 116) Benzo[g]quinoxalin-2-yl-(4-trifluoromethylphenyl)-amine
Rt: 3.63 min; Mol. Mass: 339

δ (ppm) = 10.70(s,1H, NH), 8.76(s, 1H, 2-H), 8.54(s, 1H, 5-H), 8.33(s, 1H, 10-H), 8.31(d, 4H, 3',5'-H), 8.13(m, 2H, 6,9-H), 7.76(d, 2H, 2',6'-H), ^{3}J=8.5Hz), 7.55(m, 2H, 7,8-H)

Example 17



General Method for the synthesis of Compounds 117-134

107 mg (0.5 mmol) 2-Chloro-3-thiophen-2-yl-benzo[g]quinoxaline was dissolved in the mixture of 2 ml 2-propanol and 3 ml DMF. 0.55 mmol amine and 0.6 ml methanol saturated with HCl was added. The reaction mixture was stirred at 50°C for two hours then evaporated to dryness in vacuum. The residue was crystallized from ethanol-water.

(Compound 117) (5-Chloro-2-methylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine

Rt: 3.62 min; Mol. Mass: 401

δ (ppm) = 12.64(s, 1H, NH), 8.81(s, 1H, 5-H), 8.77(s, 1H, 10-H), 8.33(m, 1H, 5'-H), 8.24(m, 2H, 6,9-H,), 7.95(m, 1H, 3"-H), 7.65(m, 3H, 7,8,6"-H), 7.31(m, 3H, 3',4',4"-H)

(Compound 118) (2-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.76 min; Mol. Mass: 371

δ (ppm) = 8.78(s, 1H, NH), 8.59(s, 1H, 5-H), 8.32(s, 1H, 10-H), 8.01(m, 3H, 6,9,5'-H), 7.49(m, 2H, 7,8-H,) 7.38-7.23(m, 6H, 3',4',3",4",5",6"-H)

(Compound 119) (4-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine

Rt: 3.85 min; Mol. Mass: 421

δ (ppm) = 9.47(s, 1H, NH), 8.54(s, 1H, 5-H), 8.30(s, 1H, 10-H), 8.04(m, 5H, 6,9,5',3",5"-H), 7.89(d, 1H, 3'-H, ^{3}J=3.5H$_2$), 7.71(d, 2H, 2",6"-H, ^{3}J=8.9H$_2$), 7.53(m, 2H, 7,8,-H), 7.30(m, 1H, 4'-H)

(Compound 120) (3,4-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

107 mg (0.5 mmol) 2-Chloro-3-thiophen-2-yl-benzo[g]quinoxaline was dissolved in the mixture of 2 ml 2-propanol and 3 ml DMF. 85 mg (0.55 mmol) amine and 0.6 ml methanol saturated with HCl was added. The reaction mixture was stirred at 50°C for two hours then evaporated to dryness in vacuum. The residue was crystallized from ethanol-water.

Yield: 127 mg (77%)

Rt: 3.56 min; Mol. Mass: 414

δ (ppm) = 8.90(s, 1H, NH), 8.46(s, 1H, 5-H), 8.10(s, 1H, 10-H), 7.96(m, 4H, 6,9,5',5"-H), 7.47(m, 4H, 7,8,3',2"-H), 7.31(m, 1H, 4'-H), 6.97(d, 1H, 6"-H, $^3J=7.8H_2$)

(Compound 121) (2,5-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.85 min; Mol. Mass: 414

δ (ppm) = 8.76(s, 1H, NH), 8.75(s, 1H, 5-H), 8.53(s, 1H, 10-H), 8.31(s, 1H, 6"-H), 8.13(d, 1H, 5"-H, $^3J=8.5H_2$), 8.01(m, 3H, 5',6,9-H), 7.52(m, 2H, 7,8,-H), 7.41(m, 1H, 3'-H), 7.04(d, 1H, 4"-H), 6.66(m, 1H, 4'-H), 3.85(s, 3H, CH_2), 3.84(s, 3H, CH_2)

(Compound 122) (4-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.83 min; Mol. Mass: 388

δ (ppm) = 9.49(s, 1H, NH), 8.49(s, 2H, 5,10-H), 8.04(m, 3H, 5',6,9-H), 7.92(d, 2H, 3",5"-H, $^3J=8.9H_2$), 7.47(m, 4H, 7,8,2",6"-H), 7.31(m, 2H, 3',4'-H)

(Compound 123) (3-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.74 min; Mol. Mass: 371

δ (ppm) = 9.26(s, 1H, NH), 8.57(s, 1H, 5-H), 8.34(s, 1H, 10-H), 8.01(m, 3H, 2',6,9-H), 7.92(d, 1H, 5"-H, $^3J=3.4H_2$), 7.57-7.27(m, 5H, 7,8,4',5',6'-H), 6.91(m, 1H, 4'-H)

(Compound 124) (3-Hydroxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.55 min; Mol. Mass: 369

δ (ppm) = 9.40(s, 1H, NH), 8.90(s, 1H, OH), 8.53(s, 1H, 5-H), 8.23(s, 1H, 10-H), 8.05(m, 2H, 6,9-H), 7.91(d, 1H, 5"-H, $^3J=3.5H_2$), 7.51(m, 3H, 7,8,2'-H), 7.32(m, 2H, 6',3"-H), 7.16(m, 1H, 5'-H), 6.52(d, 1H, 4'-H, $^3J=7.9H_2$)

(Compound 125) N-[4-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide

Rt: 3.46 min; Mol. Mass: 411

δ (ppm) = 9.97(s, 1H, NH), 9.05(bs, 1H, NH), 8.46(s, 1H, 5-H), 8.19(s, 1H, 10-H), 8.05(m, 2H, 6,9-H), 7.91(d, 1H, 5"-H, $^3J=3.5H_2$), 7.81(d, 2H, 3',5'-H, $^3J=8.9H_2$), 7.61(d, 3H, 2',6',3"-H), 7.49(m, 2H, 7,8-H), 7.31(m, 1H, 4"-H)

(Compound 126) (2-Hydroxy-4-methylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.86 min; Mol. Mass: 383

δ (ppm) = 10.19(s, 1H, NH), 8.72(s, 1H, OH), 8.64(s, 1H, 5-H), 8.28(s, 1H, 10-H), 8.06(m, 4H, 6,9,5",3"-H), 7.52(m, 2H, 7,8-H), 7.35(m, 1H, 4"-H), 6.76(m, 3H, 3',5',6'-H)

(Compound 127) (3-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.85 min; Mol. Mass: 388

δ (ppm) = 9.24 (s, 1H, NH), 8.52 (s, 1H, 5-H), 8.27 (s, 1H, 10-H), 8.13-7.88 (m, 4H, 6,9,5",2'-H), 7.57-7.13(m, 7H, 7,8,4',5',6',3",4"-H),

(Compound 128) (4-Bromophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.90 min; Mol. Mass: 432

δ (ppm) = 9.19(s, 1H, NH), 8.51(s, 1H, 5-H), 8.24(s, 1H, 10-H), 8.05(m, 3H, 6,9,5"-H), 7.9(m, 3H, 3',5',3"-H), 7.60(d, 2H, 2',6'-H, $^3J=8.9H_2$), 7.51(m, 2H, 7,8-H), 7.31(m, 3H, 4"-H)

(Compound 129) (3-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.81 min; Mol. Mass: 421

δ (ppm) ($CDCl_3$) = 8.52(s, 1H, 5-H), 8.31(s, 1H, 10-H), 8.25(s, 1H, 2'-H), 8.08(d, 1H, 4'-H, $^3J=7.9Hz$), 8.02(m, 2H, 6,9-H), 7.79(d, 1H, 5"-H,

^{3}J=4.5Hz), 7.67(d, 1H, 3"-H, ^{3}J=3.5Hz), 7.58-7.45(m, 3H, 7,8,5'-H), 7.39(d, 1H, 6'-H, ^{3}J=7.6Hz), 7.29(m, 1H, 4"-H)

(Compound 130) (2-Morpholin-4-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 2.79 min; Mol. Mass: 391

δ (ppm) ($CDCl_3$) = 8.45(s, 1H, 5-H), 8.15(s, 1H, 10-H), 7.96(m, 2H, 6,9-H), 7,79(d, 1H, 5"-H, ^{3}J=4.7Hz), 7.61(d, 1H, 3"-H, ^{3}J=6.8Hz), 7.44(m, 2H, 7,8-H), 7.24(m, 1H, 4"-H), 6.65(s, 1H, NH), 3.71(m, 4H, O-CH_2), 2.75(m, 2H, CH_2), 2.48(m, 6H, N-CH_2)

(Compound 131) [3-(4-Methylpiperazin-1-yl)-propyl]-(3-thiophen-2-yl-benzo[g]-quinoxalin-2-yl)-amine

δ (ppm) = 8.40(s, 1H, 5-H), 8.09(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.95(d, 1H, 5"-H, ^{3}J=3.57Hz), 7.98(d, 1H, 3"-H, ^{3}J=5.12Hz), 7.47(m, 2H, 4"-H), 3.37(m, 2H, O-CH_2), 2.42(m, 11H, N-CH_2, N-CH_3), 2.29(s, 3H, CH_3)

(Compound 132) (2-Piperidin-1-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 2.85 min; Mol. Mass: 3.89

δ (ppm) ($CDCl_3$) = 8.44(s, 1H, 5-H), 8.14(s, 1H, 10-H), 7.95(m, 2H, 6,9-H), 7.84(d, 1H, 5"-H, ^{3}J=4.6Hz), 7.59(d, 1H, 3"-H, ^{3}J=6.8Hz), 7.44(m, 2H, 7,8-H), 7.24(m, 1H, 4"-H), 6.85(s, 1H, NH), 3.73(q, 2H, a-CH_2), 2.68(m, 2H, b-CH_2), 2.48(m, 4H, N-CH_2), 1.67-1.55(m, 6H, 3',4',5'-CH_2)

(Compound 133) N-(3-Bromophenyl)-N'-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-hydrazine

Rt: 4.31 min; Mol. Mass: 447

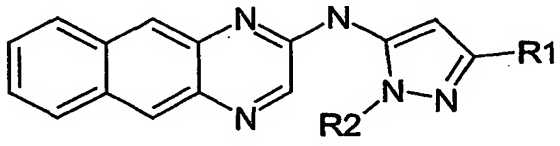
δ (ppm) = 11.40(s, 1H, NH), 8.73(b, 1H, NH), 8.34(s, 1H, 5-H), 7.99(s, 1H, 10-H), 7.87(m, 2H, 6.9-H,), 7.74(m, 1H, 5'-H), 7.57(s, 1H, 2"-H), 7.48-7.18(m, 6H, 7,8,2',3',4",5"-H), 6.89(d, 1H, 6"-H, ^{3}J=7.7Hz)

(Compound 134) (4-Butylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

Rt: 4.03 min; Mol. Mass: 410

δ (ppm) = 8.94(s, 1H, NH), 8.48(s, 1H, 5-H), 8.19(s, 1H, 10-H), 8.05(m, 2H, 6.9-H), 8.04(d, 1H, 5'-H), 7.91(d, 1H, 3'-H), 7.81(d, 2H), 7.48(m, 2H, 7.8-H), 7.30(dd, 1H, 4'-H), 7.20(d, 2H, 2",6"-H)

Example 18



General Method for the synthesis of Compounds 135-140

107 mg (0.5 mmol) 2-chlorobenzo[g]quinoxaline and (0.5 mmol) 3-amino-2H-pyrazoles were dissolved in 2 ml dimethylsulfoxide (DMSO) and 50 mg NaH was added and stirred at room temperature for 30 minutes. The product was precipitated by addition of ice water and filtered off and washed with more distilled water and dried.

(Compound 135) Benzo[g]quinoxalin-2-yl-[2-(2-bromo-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

δ (ppm) = 8.51(s, 2H, 2.5-H), 8.30(s, 1H, 10-H), 8.04(m, 2H, 6.9-H), 7.75-7.35(m, 8H, 3``,4``,5``,6``-H), 6.82(s, 1H, 4`-H), 6.71(s, 1H, NH), 1.46(s, 9H, CH_3)

(Compound 136) Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(3-nitro-phenyl)-2H-pyrazol-3-yl]-amine

Rt: 3.52 min; Mol. Mass: 438

δ (ppm) = 10.25(bs, 1H, NH), 8.66(s, 1H, 2"-H), 8.51(s, 1H, 5-H), 8.45(s, 1H, 10-H), 8.12(m, 3H, 4",6,9-H), 8.04(d, 1H, 6"-H), 7.73(t, 1H, 5"-H)

(Compound 137) Benzo[g]quinoxalin-2-yl-[2-(3-fluoro-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

δ (ppm) = 8.54(s, 1H, 2-H), 8.51(s, 1H, 5-H), 8.29(s, 1H, 10-H), 8.05(m, 2H, 6.9-H), 7.55(m, 2H, 7.8-H), 7.42(m, 2H, 4``,5``-H), 7.08(m, 3H, 2``,4``-H, NH), 6.82(s, 1H, 4`-H), 1.43(s, 9H, CH_3)

(Compound 138) Benzo[g]quinoxalin-2-yl-[2-(3-trifluoromethyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

δ (ppm) = 8.53(s, 1H, 2-H), 8.51(s, 1H, 5-H), 8.25(s, 1H, 10-H), 8.04(m, 2H, 6.9-H), 7.6-7.51(m, 6H, 7.8, 2``,4``,5``,6``-H), 7.05(s, 1H, NH), 6.77(s, 1H, 4`-H), 1.45(s, 9H, CH_3)

(Compound 139) Benzo[g]quinoxalin-2-yl-[2-(2-methyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine

δ (ppm) = 8.51(s, 1H, 2H), 8.42(s, 1H, 5-H), 8.35(s, 1H, 10-H), 8.05 (m, 2H, 6,9-H), 7.54(m, 2H, 7,8-H), 7.40(m, 4H, 3``,4``,5``,6``-H), 6.98(s, 1H, 4`-H), 6.68(s, 1H, NH), 2.18(s, 3H, CH_3), 1.46(s, 9H, -CH_3)

(Compound 140) Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(4-nitro-phenyl)-2H-pyrazol-3-yl]-amine

δ (ppm) = 8.55(s, 1H, 2-H), 8.53(s, 1H, 5-H), 8.30(d, 2H, 3``,5``-H, 6, ^3J=8.4 Hz), 8.22(s, 1H, 10-H), 8.04(m, 2H, 6.9-H), 7.92(d, 2H, 2``,6``-H), 7.55(m, 2H, 7.8-H), 6.70(s, 1H, 5`-H), 1.44(s, 9H, -CH_3)

Example 19

General Method for the synthesis of Compounds 141-144

125 mg (0.5 mmol) 2,3-Dichlorobenzo[g]quinoxaline and (0.5 mmol) 3-amino-2H-pyrazoles were dissolved in 2 ml DMSO and 50 mg NaH was added and stirred at room temperature for 30 minutes. The product was precipitated by addition of ice water and filtered off and washed with more distilled water and dried.

(Compound 141) [5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-(3-chloro-benzo[g]-quinoxalin-2-yl)-amine

Rt: 3.62; Mol. Mass: 427

δ (ppm) = 9.43(s, 1H, NH), 8.46(s, 1H, 5-H), 8.19(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.61-7.18(m, 7H, 7,8-H, phenyl-H), 6.59(s, 1H, 4'-H), 1.37(s, 9H, CH_3)

(Compound 142) [5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.58; Mol. Mass: 457

δ (ppm) = 9.29(s, 1H, NH), 8.47(s, 1H, 5-H), 8.23(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.54(m, 4H, 7,8,3",5"-H), 6.93(d, 2H, 2",6"-H, ^{3}J=8.9Hz), 6.55(s, 1H, 4'-H), 3.68(s, 3H, -CH_3), 1.36(s, 9H, -CH_3)

(Compound 143) [5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

1.24 g (5 mmol) 2,3-Dichlorobenzo[g]quinoxaline and 1.3 g (5 mmol) 3-Amino-5-tert-butyl-2-(3-nitro-phenyl)-2H-pyrazol were dissolved in 20 ml DMSO and 0.5 g NaH was added and stirred at room temperature for 30 minutes. The product was precipitated by addition of ice water and filtered off and washed with more distilled water and dried.

Yield: 2.05 g (95%)

Rt: 3.60 min; Mol. Mass: 472

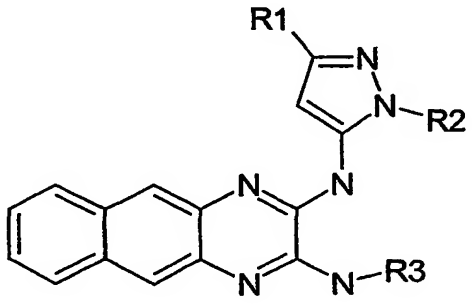
δ (ppm) = 9.71(s, 1H, NH), 8.48(s, 1H, 5-H), 8.44(s, 1H, 2"-H), 8.15(s, 1H, 10-H), 8.06(m, 4H, 6,9,4",5"-H), 7.69-7.49(m, 3H, 7,8,6"-H), 6.66(s, 1H, 4'-H), 1.39(s, 9H, -CH_3)

(Compound 144) [5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.64 min; Mol. Mass: 445

δ (ppm) = 9.54(s, 1H, NH), 8.47(s, 1H, 5-H), 8.18(s, 1H, 10-H), 8.07(m, 2H, 6,9-H), 7.59-7.40(m, 4H, 7,8,5",6"-H), 7.06(m, 1H, 4"-H), 6.62(s, 1H, 4'-H), 1.37(s, 9H, CH_3)

Example 20



General Method for the synthesis of Compounds 145-171

0.5 mmol of the substituted 2-amino-3-chloro-benzo[g]quinoxalines and 1.0 mmol appropriate amines were refluxed overnight in 5 ml i-propanol. The products were precipitated by addition of water or 1 N hydrochloric acid (HCl) or

5% $NaHCO_3$. The precipitates were filtrated and washed with distilled water then diethylether.

(Compound 145) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 2.86 min; Mol. Mass: 516

δ (ppm) = 10.93(s, 1H, NH), 7.85-7.75(m, 5H, 5,6,9,10-H, NH), 7.50-7.22(m, 8H, 7,8,7'-H, phenyl 5-H), 6.90(s, 1H, 8'-H), 6.30(s, 1H, 4"-H), 4.05(m, 2H, 3'-H_2), 3.48(m, 2H, 1'-H_2), 2.09(m, 2H, 2'-H_2), 1.37(s, 9H, CH_3)

(Compound 146) 2-(3-([5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

Rt: 3.4 min; Mol. Mass: 497

δ (ppm) = 11.02, 8.68(s, 2H, NH), 8.20(m, 2H, 6,9-H), 7.87-7.69(m, 4H, 2"',4"',5"',6"'-H), 7.35(m, 2H, 7,8-H), 6.47(s, 3'-H), 4.82(bs, 1H, OH), 3.60(m, 2H, 2'-H_2), 3.30(m, 2H, 1'-H_2)

(Compound 147) 2-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

Rt: 3.32 min; Mol. Mass: 470

δ (ppm) = 11.3, 8.9(s, 2H, NH), 8.04(s, 1H, 5-H), 7.86(m, 3H, 6,9,10-H), 7.66(m, 2H, 7,8-H), 7.49(m, 3H, 2"',5"',6"'-H), 7.02(m, 1H, 4"'-H), 6.36(s, 1H, 4"-H), 3.77(m, 2H, 2'-H_2), 3.71(m, 2H, 1'-H_2), 1.37(s, 9H, -CH_3)

(Compound 148) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.85 min; Mol. Mass: 496

δ (ppm) = 11.4, 8.14(bs, 2H, NH), 7.88(m, 4H, 5,10,6,9-H), 7.65(m, 2H, 2"',6"'-H), 7.43(m, 3H, 7,8,5"'-H), 7.11(m, 1H, 4"'-H), 6.36(s,1H, 4"-H), 3.69(m, 2H, 1'- H_2), 1.70(m, 1H, 3'-H), 1.59(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3), 0.94(d, 6H, -CH_3, ^{3}J=6.5 Hz)

(Compound 149) 3-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol

Rt: 3.31 min; Mol. Mass: 484

δ (ppm) = 10.96(s, 1H, NH), 7.85-7.70(m, 4-H, 5,10,6,9-H), 7.56-7.32(m, 5H, 7,8,2‴,5‴,6‴-H), 7.07(m, 1H, 4‴-H), 6.33(s, 1H, 4'-H), 4.62(bs, 1H, OH), 3.55(m, 4H, 1',3'-H_2), 1.79(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 150) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.84 min; Mol. Mass: 548

δ (ppm) = 11.3, 8.15(bs, 2H, NH), 7.88(m, 4H, 5,10,6,9-H), 7.63-7.04(m, 10H, 7,8,2‴,4‴,5‴,6‴-H), 6.32(s, 1H, 4"-H), 3.93(m, 2H, 1'-H_2), 3.04(m, 1H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 151) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.96 min; Mol. Mass:564

δ (ppm) = 11.4, 8.17(bs, 2H, NH), 7.88(m, 4H, 5,10,6,9-H), 7.63-7.06(m, 10H, 7,8,2‴,4‴,5‴,6‴-H), 6.32(s, 1H, 4"-H), 3.90(m, 2H, 1'-H_2), 3.02(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 152) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.77 min; Mol. Mass: 560

δ (ppm) = 11.4, 8.16(bs, 2H, NH), 7.88(m, 4H, 5,10,6,9-H), 7.63(m, 2H, 2‴,6‴-H), 7.44(m, 3H, 7,8,5‴-H), 7.24(d, 2H, 5',7'-H, ^{3}J=8.5 Hz), 7.13(m, 1H, 4‴-H), 6.82(d, 2H, 4',8'-H), 6.33(s, 1H, 4"-H), 3.89(m, 2H, 1'- H_2), 2.94(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 153) 3-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol

Rt: 3.20 min Mol. Mass: 496

δ (ppm) = 10.83(bs, 1H, NH), 7.83(m, 5H, 5,10,6,9-H, NH), 7.62(d, 2H, 3‴,5‴-H, ^{3}J=8.5Hz), 7.34(m, 2H, 7,8-H), 6.93(d, 2H, 2‴,6‴-H), 6.29(s, 1H, 4‴-H), 5.70(bs, 1H, OH), 3.77(s, 3H, -CH_3), 3.53(m, 4H, 1',3'-H), 1.78(m, 2H, 2'-H),1.36(s, 9H, -CH_3)

(Compound 154) 3-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol

0.214 g (0.5 mmol) of [5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine and 0.2 ml 3-propanolamine were refluxed

overnight in 5 ml i-propanol. The product was precipitated by addition of 1 N aqueous hydrochloric acid. The precipitate was filtrated and washed with distilled water then diethylether.
Yield: 0.20 g (86%)
Rt: 3.23 min; Mol. Mass: 465
δ (ppm) = 10.3(bs, 1H, NH), 8.07(s, 1H, NH), 7.88(s, 2H, 5,10-H), 7.80(m, 2H, 6,9-H), 7.44-7.23(m, 5H, phenyl-H), 6.33(s, 1H, 4"-H), 3.71(m, 2H, 3'-H_2), 3.56(m, 2H, 1'-H_2), 1.84(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 155) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
Rt: 3.91 min; Mol. Mass:546
δ (ppm) = 10.9(bs, 1H, NH), 7.83(m, 5H, 5,6,9,10-H, NH), 7.45-7.23(m, 9H phenyl-H), 6.31(s, 1H, 4"-H), 3.76(m, 2H, 1'-H_2), 3.10(m, 2H, 2'-H_2)

(Compound 156) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
Rt: 3.70 min; Mol. Mass: 542
δ (ppm) = 8.76(s, 1H, NH), 7.93(s, 1H, 5-H), 7.80(m, 2H, 6,9-H), 7.67(s, 1H, 10-H), 7.42-7.28(m, 7H, 7,8-H, phenyl-H), 7.14(d, 2H, 5',7'-H, ^3J=8.5 Hz), 6.80(d, 2H, 4',8'-H), 6.74(bs, 1H, NH), 6.14(s, 1H, 4"-H), 3.83(m, 2H, 1'-H_2), 3.79(s, 3H, -CH_3), 2.93(m, 2H, 2'-H_2), 1.45(s, 9H, -CH_3)

(Compound 157) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.73 min; Mol. Mass: 502
δ (ppm) ($CDCl_3$) = 8.96(s, 1H, NH), 8.15(s, 1H, 5-H), 7.96(m, 3H, 6,9,10-H), 7.61-7.39(m, 7H, 7,8-H, phenyl-H), 7.09(bs, 1H, NH), 6.39(s, 1H, 3'-H), 6.39(s, 1H, 4"-H), 6.14(s, 1H, 4'-H), 4.94(s, 2H, CH_2), 2.38(s, 3H, -CH_3), 1.46(s, 9H, -CH_3)

(Compound 158) 2-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-ethanol
Rt: 3.23; Mol. Mass: 482
δ (ppm) = 11.4(bs, 1H, NH), 8.22(s, 1H, NH), 7.88(m, 3H, 6,9,10-H), 7.63-7.42(m, 4H, 7,8,3"',5"'-H), 6.96(d, 2H, 2"',6"'-H, ^3J=8.5Hz), 6.34(s, 1H, 4"-H), 4.0(bs, 1H, OH), 3.71(m, 2H, 2'-H_2), 3,68(m, 2H, 1'-H_2), 1.37(s, 9H, -CH_3)

(Compound 159) N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.69 min; Mol. Mass: 508
δ (ppm) = 11.3(bs, 1H, NH), 7.89(m, 4H, 5,6,9,10-H), 7.62-7.42(m, 4H, 7,8,3''',5'''-H), 6.95(d, 2H, 2''',6'''-H, ^{3}J=8.5Hz), 6.35(s, 1H, 4''-H), 3.93(bs, 1H, OH), 3.68(m, 2H, 1'-H), 1.68(m, 1H, 3'-H), 1.57(m, 2H, 2'-H), 1.37(s, 9H, -CH_3), 0.95(d, 6H, -CH_3, ^{3}J=6.5Hz)

(Compound 160) N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 2.86 min; Mol. Mass: 546
δ (ppm) = 8.84(s, 1H, NH), 7.81(m, 4H, 5,6,9,10-H), 7.57-7.40(m, 7H, 7,8,5',7',8',3''',5'''-H), 6.95(d, 2H, 2''',6'''-H, ^{3}J=8.5Hz), 6.69(bs, 1H, NH), 6.15(s, 1H, 4''-H), 4.04(m, 2H, 3'-H_2), 3.82(s, 3H, -CH_3), 3.60(m, 2H, 1'-H_2), 2.17(m, 2H, 2'-H_2), 1.45(s, 9H, -CH_3)

(Compound 161) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
Rt: 3.98 min; Mol. Mass: 564
δ (ppm) = 11.3, 8.03(bs, 2H, NH), 7.86(m, 4H, 5,6,9,10-H), 7.63-7.23(m, 9H, 7,8,5',6',7',8',2''',4'''5''',6'''-H), 6.31(s, 1H, 4''-H), 4.13(m, 2H, 1'-H_2), 3.15(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 162) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.06 min; Mol. Mass: 534
δ (ppm) = 11.5, 8.08(bs, 2H, NH), 7.84(m, 4H, 5,6,9,10-H), 7.84-7.36(m, 5H, 7,8,2''',5''',6'''-H), 7.11(m, 1H, 4'''-H), 6.35(s, 1H, 4''-H), 5.43(s, 1H, 4'-H), 3.72(m, 2H, 1'-H_2), 2.30(bs, 2H, 2'-H_2), 1.82, 1.57, 1.53, 1.42(bs, 8H, 5',6',7',8'-H_2)

(Compound 163) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine
Rt: 3.21; Mol. Mass: 517
δ (ppm) = 11(bs, 1H, NH), 8.68(s, 1H, 3'-H), 8.46(d, 1H, 5'-H, ^{3}J=3.8Hz), 8.17(bs, 1H, NH), 7.78(m, 7H, 6,9,5,10,6',7',6'''-H), 7.38(m, 4H,

7,8,2‴, 5‴-H), 7.05(m, 1H, 4‴-H), 6.35(s, 1H, 4"-H), 4.73(bs, 2H, 1'-H_2), 1.36(s, 9H, -CH_3)

(Compound 164) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.79 min; Mol. Mass: 520
δ (ppm) = 11.3, 8.17(bs, 2H, NH), 7.58(m, 4H, 5,6,9,10-H), 7.65(m, 2H, 2",6"-H), 7.44(m, 3H, 7,8,5‴-H), 7.08(m, 1H, 4‴-H), 6.36(s, 2H, 3',4'-H), 6.03(s, 1H, 4"-H), 4.80(s, 2H, 1'-H_2), 1.37(s, 9H, -CH_3)

(Compound 165) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 2.86 min; Mol. Mass: 534
δ (ppm) = 10.99(s, 1H, NH), 7.85-7.66(m, 7H, 5,6,9,10,5',2‴,NH), 7.48-7.32(m, 4H, 7,8,5‴,6‴-H), 7.22(s, 1H, 6'-H), 7.04(m, 1H, 4‴-H), 6.90(s, 1H, 7'-H), 6.31(s, 1H, 4"-H), 4.07(m, 2H, 3'-H_2), 3.49(m, 2H, 1'-H_2), 2.11(m, 2H, 2'-H_2), 1.37(s, 9H, -CH_3)

(Compound 166) 2-[(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-amino(-benzo[g]quinoxalin-2-yl)-(2-hydroxyethyl)-amino]-ethanol
Rt: 2.83 min; Mol. Mass: 514
δ (ppm) = 11.2(bs, 1H, NH), 8.18(s, 1H, 5-H), 8.00(m, 4H, 6,9,10-H, NH), 7.46(m, 5H, 7,8,2‴, 5‴,6‴-H), 7.06(m, 1H, 4‴-H), 6.63(s, 1H, 4"-H), 4.58(bs, 2H, OH), 3.79(m, 4H, 2'-H_2), 3.03(bs, 2H, 1'-H_2), 2.69(bs, 2H, 1'-H_2), 1.37(s, 9H, -CH_3)

(Compound 167) N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-4-yl-methyl-benzo[g]quinoxaline-2,3-diamine
Rt: 3.08 min; Mol. Mass: 517
δ (ppm) = 11.06(s, 1H, NH), 8.51(d, 2H, 4',6'-H, ^3J=4.9Hz), 8.24(bs, 1H, NH), 7.76(m, 6H, 5,6,9,10,3',7'-H), 7.39(m, 5H, 7,8,2‴,5‴,6‴-H), 7.06(m, 1H, 4‴-H), 6.31(s, 1H, 4"-H), 4.75(bs, 2H, 1'-H_2), 3.30(bs, 2H, 2'-H_2), 1.38(s, 9H, -CH_3)

(Compound 168) N-(1-Benzylpiperidin-4-yl-methyl)-N'-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-benzo[g]quinoxaline-2,3-diamine
Rt: 2.97 min; Mol. Mass: 599

δ (ppm) = 7.95-7.11(m, 15H, 5,6,9,10,2',3',4',5',6',2''',3''',4''',5''',6'''-H,NH), 6.47(s, 1H, 4"-H), 3.48(s, 2H, CH_2), 2.69, 2.21, 1.95, 1.63(bs, 8H, piperidine-H), 1.37(s, 9H, -CH_3)

(Compound 169) 2-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

Rt: 3.25 min; Mol. Mass: 452

δ (ppm) = 11.4(bs, 1H, NH), 8.09(s, 1H, NH), 7.87(m, 4H, 5,6,9,10-H), 7.75(m, 2H, 7,8-H), 7.43(m, 5H, aromatic ring), 6.36(s, 1H, 4"-H), 4.03(m, 2H, 2'-H_2), 3.70(m, 2H, 1'-H_2), 1.37(s, 9H, -CH_3)

(Compound 170) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.75 min; Mol. Mass: 478

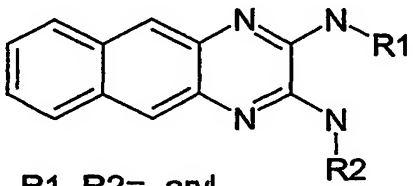
δ (ppm) = 10.4(bs, 1H, NH), 8.14(s, 1H, NH), 7.91(s, 2H, 5,10-H), 8.87(m, 2H, 6,9-H), 7.40(m, 2H, 7,8-H), 7.46-7.24(m, 5H, phenyl-H), 6.35(s, 1H, 4"-H), 3.68(m, 2H, 1'-H2), 1.67(m, 1H, 3'-H), 1.58(m, 2H, 2'-H), 1.37(s, 9H, CH_3), 0.94(d, 6H, CH_3, ^3J=6.4Hz)

(Compound 171) N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.96 min; Mol. Mass: 516

δ (ppm) ($CDCl_3$) = 9.56(bs, 1H, NH), 8.74(bs, 1H, NH), 7.85(m, 2H, 6,9-H), 7.67-7.20(m, 9H, 5,7,8,10-H, phenyl-H), 7.07(bs, 1H, 5"-H), 5.15(s, 1H, 4'-H), 3.88(bs, 2H, 1'-H_2), 2.18(bs, 2H, 2'-H_2), 1.87, 1.70, 1.55, 1.41(bs, 8H, CH_2 ring), 1.37(s, 9H, CH_3)

Example 21



R1, R2= aryl

General Method for the synthesis of Compounds 172-205

2,3-Dichloro-benzo[g]quinoxaline (0.32 mmol) and the appropriate aromatic amine (1.28 mmol) was heated overnight in 15 ml of isopropyl alcohol. The

solution was enhanced by adding a few drops of DMF if necessary. After cooling, the precipitated crystals were filtered off, washed with propanol and dried under vacuum.

(Compound 172) N,N'-Dipyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine
Rt:2.51 min; Mol. Mass: 392
δ (ppm) = 10.2(bs, 2H, NH), 8.52(m, 4H, 2``, 6``-H), 8.02(s, 2H, 5, 10-H), 7.88(m, 2H, 6,9-H), 7.67-7.38(m, 6H, 7, 8, 3``, 4``-H), 3.67(s, 4H, 1`-H_2)

(Compound 173) N,N'-Diphenyl-benzo[g]quinoxaline-2,3-diamine
Rt: 3.75 min.; Mol. Mass.: 362
δ (ppm) = 8.06(s, 2H, 5, 10-H), 7.98(m, 8H, 6, 9, 3', 5'-H, NH), 7.41(m, 6H, 7, 8, 2', 6'-H), 7.15(m, 2H, 4'-H)

(Compound 174) N,N'-Bis-[1,2,4]triazol-4-yl-benzo[g]quinoxaline-2,3-diamine
2,3-Dichloro-benzo[g]quinoxaline (0.32 mmol) and 4-amino-1,2,4-triazole (1.28 mmol) was heated overnight in 15 ml of isopropyl alcohol. The solution was enhanced by adding a few drops of DMF if neccesary. After cooling, the precipitated crystals were filtered off, washed with propanol and dried under vacuum.
Yield: 72%
Rt: 2.72 min; Mol. Mass: 344.34
δ (ppm) = 11.27(s, 2H, NH), 8.76(s, 4H, 2', 4'-H), 7.81(m, 4H, 5, 10, 6, 9-H), 7.40(m, 2H, 7, 8-H)

(Compound 175) N,N'-Bis-(4-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.38 min.; Mol. Mass.: 431.33
δ (ppm) = 8.05(s, 2H, 5, 10-H), 8.01(d, 4H, 3', 5'-H, ^{3}J=8.8Hz), 8(bs, 2H, NH), 7.96(m, 2H, 6, 9-H), 7.48(d, 4H, 2', 6'-H), 7.41(m, 2H, 7, 8-H)

(Compound 176) N,N'-Bis-(4-bromophenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.57 min.; Mol. Mass.: 520
δ (ppm) = 8.05(s, 2H, 5, 10-H), 7.97(m, 8H, 6, 9, 3', 5'-H, NH), 7.60(d, 4H, 2', 6'-H ^{3}J=8.8Hz), 7.41(m, 2H, 7, 8-H)

(Compound 177) N,N'-Bis-(4-phenoxyphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.45 min; Mol. Mass: 546
δ (ppm) = 9.9(b, 2H, NH), 8.03(m, 2H, 5, 10-H), 7.95(m, 2H, 6, 9-H), 7.40(m, 6H, 7, 8, 2", 6"-H), 7.12(m, 14H, 2', 3', 5', 6', 3", 4", 5"-H)

(Compound 178) N,N'-Bis-(3,4-dimethyl-phenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.26 min.; Mol. Mass.: 418
δ (ppm) = 9.8(b, 2H, NH), 8.02(s, 2H, 5, 10-H), 7.94(m, 2H, 6, 9-H), 7.70(d, 2H, 6'-H, ^{3}J=8.2Hz), 7.65(s, 2H, 2'-H), 7.40(m, 2H, 7, 8-H), 7.22(d, 2H, 5'-H), 2.30(s, 6H-CH_3), 2.26(s, 6H, -CH_3)

(Compound 179) N,N'-Bis-(4-methylsulfanylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.17 min.; Mol. Mass.: 454
δ (ppm) = 9.7(b, 2H, NH), 8.02(s, 2H, 5, 10-H), 7.95(m, 4H, 6, 9-H), 7.37(m,6H, 7, 8, 3', 5', -H), 7.24(d, 4H, 2', 6'-H, ^{3}J=8.5Hz), 2.51(s, 3H, -CH_3), 2.47(s, 3H, -CH_3)

(Compound 180) N,N'-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.90 min.; Mol. Mass.: 422
δ (ppm) = 9.23(s, 2H, NH), 8.09(s, 2H, 5, 10-H), 7.95(m, 2H, 6, 9-H), 7.78(s, 2H, 2'-H), 7.51(d, 2H, 4'-H, ^{3}J=7.7Hz), 7.41(m, 2H, 7, 8-H), 7.31(t, 2H, 5'-H), 6.71(d, 2H, 6'-H, ^{3}J=6.9Hz), 3.84(s, 6H, -CH_3)

(Compound 181) N,N'-Bis-(3-chloro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.93 min.; Mol. Mass.: 459
δ (ppm) = 8.20(s, 2H, NH), 8.05(s, 2H, 5, 10-H), 7.98(m, 4, 6, 9, 5'-H), 7.85(d, 2H, 6'-H, ^{3}J=7.5Hz), 7.41(m, 4H, 7, 8, 2'-H), 2.35(s, 6H,-CH_3)

(Compound 182) N,N'-Bis-(3-bromophenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.45 min.; Mol. Mass.: 520
δ (ppm) = 8.33(s, 2H, NH), 8.08(s, 2H, 5, 10-H), 7.98(m, 6H, 6, 9, 2', 4'-H), 7.41(m, 4H, 7, 8, 5'-H), 7.30(d, 2H, 6'-H, ^{3}J=8.2Hz)

(Compound 183) N,N'-Bis-(3-fluorophenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.92 min.; Mol. Mass.: 398
δ (ppm) = 8.12(s, 4H, 5, 10-H, NH), 7.96(m, 4H, 6, 9, 4'-H), 7.80(s, 2H, 2'-H), 7.43(m, 4H, 7, 8, 6'-H), 6.94(m, 2H, 5'-H)

(Compound 184) N,N'-Bis-(3-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 3.93 min.; Mol. Mass.: 390
δ (ppm) = 11(b, 2H, NH), 8.06(s, 2H, 5, 10-H), 7.96(m, 2H, 6, 9-H), 7.81(d, 2H, 4'-H, ^{3}J=8.0Hz), 7.74(s, 2H, 2'-H), 7.41(m, 2H, 7, 8-H), 7.34(t, 2H, 5'-H), 7.00(d, 2H, 6'-H. ^{3}J=7.5Hz)

(Compound 185) N,N'-Bis-(3-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.27 min.; Mol. Mass.: 431
δ (ppm) = 8.2(s, 2H, NH), 8.06(s, 2H, 5, 10-H), 7.96(m, 4H, 6, 9, 4'-H), 7.41(m, 6H, 7, 8, 5', 2'-H), 7.15(d, 2H, 6'-H, ^{3}J=7.9Hz)

(Compound 186) N,N'-Bis-(4-ethylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.10 min.; Mol. Mass.: 418
δ (ppm) = 10.5(b, 2H, NH), 8.04(s, 2H, 5, 10-H), 7.94(m, 2H, 6, 9-H), 7.84(d, 4H, 3', 4'-H, ^{3}J=8.3Hz), 7.40(m, 2H, 7, 8-H), 7.29(d, 4H, 2', 5'-H), 2.63(q, 4H, -CH_2-), 1.22(t, 6H, -CH_3)

(Compound 187) N,N'-Bis-(4-butylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.86 min; Mol. Mass: 474.65
δ (ppm) = 8.01(s, 2H, 5, 10-H), 7.93(m, 2H, 6, 9-H), 7.83(d, 4H, 3', 4'-H, ^{3}J=8.5Hz), 7.39(m, 2H, 7, 8-H), 7.3(s, 2H, NH), 7.25(d, 2H, 2', 6'-H), 2.60(m, 4H, -CH_2-), 1.57(m, 4H, -CH_2-), 1.30(m, 4H, -CH_2-), 0.91(t, 6H, -CH_3)

(Compound 188) N,N'-Bis-(3-trifluoromethylphenyl)-benzo[g]quinoxaline-2,3-diamine
Rt: 4.09 min.; Mol. Mass.: 498
δ (ppm) = 11(b, 2H, NH), 8.47(s, 2H, 2'-H), 8.35(d, 2H, 4'-H, ^{3}J=8.1Hz), 8.06(s, 2H, 5, 10-H), 7.99(s, 2H, 6, 9-H), 7.65(t, 2H, 5'-H, ^{3}J=6.4Hz), 7.42(m, 4H, 7, 8, 6'-H)

(Compound 189) N,N'-Bis-(3,4-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.46 min.; Mol. Mass.: 482

δ (ppm) = 9.8(b, 2H, NH), 8.00(s, 2H, 5, 10-H), 7.91(m, 2H, 6, 9-H), 7.61(s, 2H, 2'-H), 7.40(m, 4H, 7, 8, 6'-H), 7.20(d, 2H, 5'-H, ^{3}J=8.7Hz), 3.82(s, 3H, -CH_3), 3.79(s, 3H, -CH_3)

(Compound 190) N,N'-Bis-(3-fluoro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 4.12 min.; Mol. Mass.: 426

δ (ppm) = 8.06(s, 2H, 5, 10-H), 7.96(m, 4H, 6, 9, 2'-H), 7.64(d, 2H, 6'-H, ^{3}J=8.2Hz), 7.40(m, 2H, 7, 8-H), 7.30(t, 2H, 5'-H, $^4J_{H,F}$=8.3Hz), 2.24(s, 6H, -CH_3)

(Compound 191) N,N'-Bis-(4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.91 min.; Mol. Mass.: 390

δ (ppm) = 8.45(b, 2H, NH), 8.03(s, 2H, 5, 10-H), 7.83(d, 4H, 3', 5'-H, ^{3}J=8.1Hz), 7.40(m, 2H, 7, 8-H), 7.25(d, 4H, 2', 6'-H), 2.33(s, 6H, -CH_3)

(Compound 192) N,N'-Bis-(2,5-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine.

Rt: 3.64 min.; Mol. Mass.: 482

δ (ppm) = 9.66(s, 2H, NH), 8.01(s, 2H, 5, 10-H), 7.34(m, 2H, 6, 9-H), 7.00(m, 2H, 7, 8-H), 6.69(d, 2H, 3'-H, ^{3}J=8.9Hz), 6.60(d, 2, 4'-H), 6.59(s, 2H, 6'-H)

(Compound 193) N-{4-[3-(4-Acetylaminophenylamino)-benzo[g]quinoxalin-2-yl-amino]-phenyl}-acetamide

Rt: 3.25 min; Mol. Mass: 476

δ (ppm) = 10.01(s, 2H, NH), 8.03(s, 2H, 5, 10-H), 7.91(m, 2H, 6, 9-H), 7.85(d, 4H, 3', 5'-H, ^{3}J=8.5Hz), 7.64(d, 4H, 2', 6'-H), 7.39(m, 2H, 7, 8-H)

(Compound 194) N,N'-Bis-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.17 min; Mol. Mass: 350

δ (ppm) = 10.2 (b, 2H, NH), 8.00(m, 2H, 6,9-H), 7.36(m, 2H, 7 8-H) 3.68(m, 4H, 1'-H_2), 1.67(m, 2H, 3'-H), 1.57(m, 4H, 2`-H_2)

(Compound 195) N,N'-Bis-(2-hydroxyethyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 2.53 min; Mol. Mass: 298

δ (ppm) = 8.80(bs, 2H, NH), 8.16(s, 2H, 5,10-H), 7.90(m, 2H, 6,9-H), 7.43(m, 2H, 7,8-H), 5.5(bs, 2H, OH), 3.90(m, 2H, 2'-H), 3.15(m, 2H, 1'-H)

(Compound 196) N,N'-Bis-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.46 min; Mol. Mass: 398

δ (ppm) = 8.92(bs, 2H, NH), 8.15(s, 2H, 5,10-H), 7.95(m, 2H, 6,9-H), 7.45(m, 2H, 7,8-H), 6.40(s, 2H, 3"-H), 6.04(s, 2H, 4"-H), 3.77(s, 4H, 1'-H_2), 2.24(s, 6H, -CH_3)

(Compound 197) N,N'-Bis-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.44 min; Mol. Mass: 454

δ (ppm) = 8.99(bs, 2H, NH), 7.99(s, 2H, 5,10-H), 7.89(m, 2H, 6,9-H), 7.46-7.10(m, 10H, 7,8,2",4",5",6"-H), 3.60(m, 4H, 1'-H_2), 3.03(m, 4H, 2'-H_2)

(Compound 198) N,N'-Bis-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.65 min; Mol. Mass:486

δ (ppm) = 8.03(bs, 2H), 7.98(s, 2H), 7.90(m, 2H), 7.43-7.26(m, 10H), 3.77(m, 4H), 3.03(m, 4H)

(Compound 199) N,N'-Dipyridin-4-yl-benzo[g]quinoxaline-2,3-diamine

Rt: 2.45 min; Mol. Mass: 392

δ (ppm) = 9.40(bs, 2H, NH), 8.52(d, 4H, 3",5"-H, ^3J=4.9Hz), 7.85(s, 2H, 5,10-H), 7.82(m, 2H, 6,9-H), 7.43(d, 4H, 2",6"-H), 7.29(m, 2H, 7,8-H), 4.79(bs, 4H, 1'-H_2)

(Compound 200) N,N'-Bis-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.23 min; Mol. Mass: 478

δ (ppm) = 8.90(b, 2H, NH), 7.90(s, 2H, 5,10-H), 7.89(m, 2H, 6,9-H), 7.35(m, 2H, 7,8-H), 7.23(d, 4H, 3",5"-H, ^3J=8.5Hz), 3.60(m, 4H, 1'-H_2), 2.78(m, 4H, 2'-H_2)

(Compound 201) N,N'-Bis-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

Rt: 3.70 ; Mol. Mass: 486

δ (ppm) = 8.85(b, 2H, NH), 7.97(s, 2H, 5,10-H), 7.90(m, 2H, 6,9-H), 7.45-7.25(m, 10H, 7,8,3",4",5",6"-H), 3.70(m, 4H, 1'-H_2), 2.78(m, 4H, 2'-H_2)

(Compound 202) N,N'-Bis-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 3.53 min; Mol. Mass: 426

δ (ppm) = 8.95(b, 2H, NH), 7.88(s, 2H, 5,10-H), 7.88(m, 2H, 6,9-H), 7.30(m, 2H, 7,8-H), 5.15(s, 1H, 4'-H), 1.87, 1.63, 1.55, 1.41(bs, 8H, CH_2)

(Compound 203) N,N'-Bis-(1-benzylpiperidin-4-yl)-benzo[g]quinoxaline-2,3-diamine

Rt: 2.64 min; Mol. Mass: 556

δ (ppm) = 9.80(b, 2H, NH), 7.98(s, 2H, 5, 10-H), 7.88(m, 2H, 6,9-H), 7.35-7.28(m, 12H, 7, 8, phenyl-H), 3.42(m, 12H, N-CH, N-CH_2), 2.31 (m, 10H, CH_2)

(Compound 204) N,N'-Bis-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 0.62 min; Mol. Mass: 426

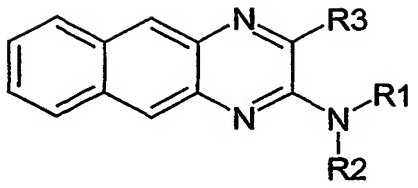
δ (ppm) = 10.9(b, 2H, NH), 7.83(s, 2H, 5,10-H), 7.70(m, 4H, 6, 9, 2``-H), 7.34(m, 2H, 7, 8-H), 7.22(s, 2H, 4``-H), 6.90(s, 2H, 5``-H), 3.28(m, 4H, 1`-$H_2$), 2.31(m, 4H, 3`-H_2), 1.89(m, 4H, 2`-H)

(Compound 205) N,N'-Bis-(3-hydroxypropyl)-benzo[g]quinoxaline-2,3-diamine

Rt: 2.56 min; Mol. Mass:326

δ (ppm) = 10.9(bs, 2H, NH), 7.96(s, 2H, 5, 10-H), 7.76(m, 2H, 6,9-H), 7.34(m, 2H, 7,8-H), 5.28(bs, 2H, OH), 3.88(m, 4H, 3`-$H_2$), 3.18(m, 4H, 1`-H_2)

Example 22



R_3=H, 2-thienyl

General Method for the synthesis of Compounds 206-213

107 mg (0.5 mmol) 2-Chloro-benzo[g]quinoxaline and 1.0 mmol amin base were heated at 100°C for 1h. The reaction mixture was poured over water-ice (10 ml) and stirred for 30 min. The obtained yellow precipitate was filtered and washed with water and diisopropylether.

(Compound 206) 2-Piperidin-1-yl-benzo[g]quinoxaline
Rt: 3.18 min.; Mol. Mass. 263.65
Melting point: 157-158°C

(Compound 207) 1-Benzo[g]quinoxalin-2-yl-piperidine-4-carboxylic acid ethyl ester
Rt: 3.33; Mol. Mass. 335.41
Melting point: 89-90°C

(Compound 208) 2-Morpholin-4-yl-benzo[g]quinoxaline
Rt: 3.09; Mol. Mass. 265.32
Melting point: 151-152°C

(Compound 209) 2-(4-Methyl-piperazin-1-yl)-benzo[g]quinoxaline
Rt: 2.38; Mol. Mass.278.36
Melting point: 120-121°C

(Compound 210) 4-Benzo[g]quinoxalin-2-yl-piperazine-1-carboxylic acid ethyl ester
Rt: 3.25; Mol. Mass. 336.40
Melting point: 136-137°C

(Compound 211) 2-(4-Phenyl-piperazin-1-yl)-benzo[g]quinoxaline
Rt: 3.53; Mol. Mass. 340.43
Melting point: 249-250°C

(Compound 212) 2-Morpholin-4-yl-3-thiophen-2-yl-benzo[g]quinoxaline
Rt: 3.67; Mol. Mass. 347.44
Melting point: 130-131°C

(Compound 213) 1-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl)-piperidine-4-carboxylic acid ethyl ester
Rt: 3.97; Mol. Mass. 417.53
Melting point: 140-141°C

Example 23

General Method for the synthesis of Compounds 214-219

A mixture of 2-chlor-benzo[g]quinoxaline (107 mg 0.5 mmol), amin hydrochloride (0.5 mmol), and sodium bicarbonate 84 mg (1 mmol) was stirred in ethanol (7 ml) and water (1 ml) for 5h, maintaining the temperature at 70°C. Once the reaction had finalized, water (6 ml) was added, and stirred for 30 min. The obtained yellow precipitate was filtered and washed with water and diisopropylether.

(Compound 214) 2-[4-(4-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
Rt: 3.54; Mol. Mass. 358.42
Melting point: 242-243°C

(Compound 215) 2-[4-(3-Trifluoromethyl-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
Rt: 3.72; Mol. Mass. 408.43
Melting point: 180-182°C

(Compound 216) 2-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
Rt: 3.43; Mol. Mass. 370.46
Melting point: 118-120°C

(Compound 217) 2-(4-Pyridin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline

A mixture of 2-Chlor-benzo[g]quinoxaline (107 mg, 0.5 mmol), 118 mg (0.5 mmol) 1-(2-pyridyl)piperazin dihydrochloride and sodium bicarbonate 126 mg

(1.5 mmol) was stirred in ethanol (7 ml) and water (1 ml) for 5h, maintaining the temperature at 70°C. Once the reaction had finalized, water (6 ml) was added, and stirred for 30 min. The obtained yellow precipitate was filtered and washed with water and diisopropylether.

Yield: 88mg

Rt: 2.68; Mol. Mass. 341.42

Melting point: 228-230°C

(Compound 218) 2-(4-Pyrimidin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline

Rt: 3.27; Mol. Mass. 342.41

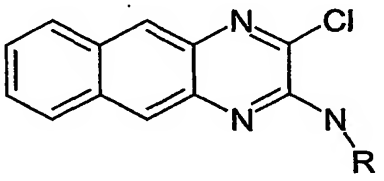
Melting point: 229-230°C

(Compound 219) 2-[4-(2-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline

Rt: 3.58; Mol. Mass. 358.42

Melting point: 139-140°C

Example 24



R=aryl

General Method for the synthesis of Compounds 220-225

0.5 mmol 2,3-Dichloro-benzo[g]quinoxaline and 0.5 mmol amino component were dissolved in 2 ml DMSO and 50 mg NaH was added and stirred at room temperature for 30 minutes. The product was precipitated by addition of ice water and filtered off and washed with more distilled water and dried.

(Compound 220) (3-Chloro-benzo[g]quinoxalin-2-yl)-(4-chlorophenyl)-amine

Rt: 3.74 min; Mol. Mass: 340.21

δ (ppm) = 8.40(s, 1H, 5-H), 8.32(s, 1H, 10-H), 8.01(m, 2H, 6, 9-H), 7.91(d, 2H, 3', 5'-H), ^{3}J=8.8Hz), 7.64(s, 1H, NH), 7.52(m, 2H, 7, 8-H), 7.41(d, 2H, 2', 6'-H)

(Compound 221) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-4-fluoro-phenyl)-amine

Rt: 4.03 min; Mol. Mass: 358

δ (ppm) = 9.36(s, 1H, NH), 8.5-8.2(m, 3H, 5, 10, 2'-H), 8.2-7.9(m, 3H, 6', 6, 9-H), 7.6-7.4(m, 3H, 5', 7, 8-H)

(Compound 222) (4-Bromo-phenyl)-(3-chloro-benzo[g]quinoxalin-2-yl)-amine

Rt: 3.69 min; Mol. Mass: 384

δ (ppm) = 9.34(s, 1H, NH), 8.47(s, 1H, 5-H), 8.29(s, 1H, 10-H), 8.2-7.9(m, 4H, 7, 8, 3', 5'-H), 7.7-7.4(m, 4H, 6, 9, 2', 6'-H)

(Compound 223) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-fluoro-phenyl)-amine

Rt: 3.55min; Mol. Mass: 323

δ (ppm) = 8.19(s, 1H, 5-H), 8.14(s, 1H, 10-H), 7.98(s, 1H, NH), 7.93(m, 1H, 2'-H), 7.9-7.7(t, 2H, 6,9-H, ^{3}J=8Hz), 7.5-7.2(m, 3H, 7, 8, 6'-H), 7.18(dd, 1H, 5'-H, ^{3}J=8Hz, ^{3}J=9Hz), 6.67(m, 1H, 4'-H)

(Compound 224) (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-phenyl)-amine

Rt: 3.66 min; Mol. Mass: 340

δ (ppm) = 9.35(s, 1H, NH), 8.48-8.31(s,s, 2H, 5,10-H), 8.21(m, 1H, 2'-H), 8.11(d, 2H, 6,9-H, ^{3}J=8.7Hz), 8.01(d, 1H, 4'-H, ^{3}J=8.1Hz), 7.54(t, 2H, 7,8-H, ^{3}J=8.7Hz), 7.43(t, 1H, 5'-H, ^{3}J=8.1Hz), 7.18(d, 1H, 6'-H, ^{3}J=8.1Hz)

(Compound 225) (3-Chloro-benzo[g]quinoxalin-2-yl)-(4-trifluoromethyl-phenyl)-amine

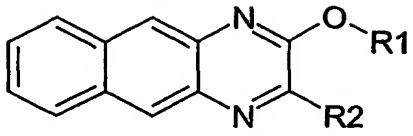
9 mmol NaH was added to a solution of 1 g (4 mmol) of 2,3-dichloro-benzo[g]quinoxalin and 0.66 g (4.1 mmol) of 4-trifluoromethylaniline. After 3 hours the red solution was quenched with ice water. The precipitated crystals are filtered off and washed with water, dried under vacuum.

Yield: 86%

Rt: 3.66 min; Mol. Mass: 373

δ (ppm) = 9.55(s, 1H, NH), 8.51(s, 1H, 10-H), 8.38(s, 1H, 5-H), 8.29(d, 2H, 3', 5'-H, ^{3}J=8.7Hz), 8.13(m, 2H, 6, 9-H, ^{3}J=8.7Hz), 7.77(d, 2H, 2', 6'-H, ^{3}J=8.7Hz), 7.57(m, 2H, 7, 8-H)

Example 25



R1= aryl
R2=H, 2-thienyl

General Method for the synthesis of Compounds 226-233

172mg (0.8 mmol) 2-Chloro-benzo[g]quinoxaline, (0.83 mmol) substituted-phenol, 115 mg (0.86 mmol) K_2CO_3 and 3 ml DMF was stirred at 60°C for 4 hours. The solvent was evaporated under reduced pressure. The residue was solidified under water. Crystals were collected by filtration, washed with water and methanol to give the named products as yellow powder.

(Compound 226) 2-(4-Chloro-phenoxy)-benzo[g]quinoxaline
Rt: 3.62 min; Mol. Mass: 306.75
δ (ppm) = 8.92(s, 1H, 3-H), 8.72(s, 1H, 5-H), 8.32(s, 1H, 10-H), 8.14(m, 2H, 6,9-H), 7.59-7.42(m, 6H, 7,8,2'3',5',6'-H)

(Compound 227) 2-(4-Bromo-phenoxy)-benzo[g]quinoxaline
Rt: 3.65 min; Mol. Mass: 351.21
δ (ppm) = 8.92(s, 1H, 3-H), 8.73(s, 1H, 5-H), 8.33(s, 1H, 10-H), 8.14(m, 2H, 6,9-H), 7.70(d, 2H, 3',5'-H, ^{3}J=8.4Hz), 7.59(m, 2H, 7,8-H), 7.38(d, 2H, 2',6'-Hz)

(Compound 228) 2-(3-Methoxy-phenoxy)-benzo[g]quinoxaline
Rt: 3.46 min; Mol. Mass: 302.34
δ (ppm) = 8.89(s, 1H, 3-H), 8.82(s, 1H, 5-H), 8.34(s, 1H, 10-H), 8.14(m, 2H, 6,9-H), 7.59(m, 3H, 7,8,2'-H), 6.95(m, 3H, 4',5',6'-H), 3.78(s, 3H, $-CH_3$)

(Compound 229) 2-(4-Methoxy-phenoxy)-benzo[g]quinoxaline
Rt:3.47 min; Mol. Mass: 302.34
δ (ppm) = 8.88(s, 1H, 3-H), 8.71(s, 1H, 5-H), 8.29(s, 1H, 10-H), 8.13(m, 2H, 6,9-H), 7.59(m, 2H, 7,8-H), 7.29(d, 2H, 2',6'-H, ^{3}J=8.3Hz), 7.04(d, 2H, 3',5'-H), 3.80(s, 3H, $-CH_3$)

(Compound 230) 2-(3,5-Dimethoxy-phenoxy)-benzo[g]quinoxaline

172 mg (0.8 mmol) 2-Chloro-benzo[g]quinoxaline, 128 mg (0.83 mmol) 3,5-dimethoxyphenol, 115 mg (0.86 mmol) K_2CO_3 and 3 ml DMF was stirred at 60°C for 4 hours. The solvent was evaporated under reduced pressure. The residue was solidified under water. Crystals were collected by filtration, washed with water and methanol to give the named products as yellow powder.

Yield: 232mg

Rt: 3.48 min; Mol. Mass: 332.36

δ (ppm) = 8.87(s, 1H, 3-H), 8.72(s, 1H, 5-H), 8.38(s, 1H, 10-H), 8.13(m, 2H, 6,9-H), 7.58(m, 2H, 7,8-H), 6.58(s, 2H, 2',6'-H), 6.47(s, 1H, 4'-H), 3.76(s, 6H, $-CH_3$)

(Compound 231) 2-(4-Bromo-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

Rt: 4.23; Mol. Mass. 433.33

Melting point: 215-217°C

(Compound 232) 2-(4-Chloro-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

Rt: 4.16; Mol. Mass. 388.88

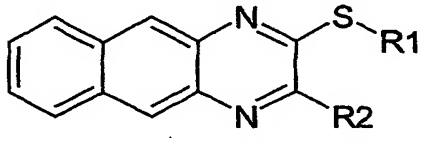
Melting point: 210-212°C

(Compound 233) 2-(3,5-Dimethoxy-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline

Rt: 3.92; Mol. Mass. 414.49

Melting point: 133-134°C

Example 26



R1= alkyl or Aryl
R2= H, 2-thienyl

General Method for the synthesis of Compounds 234-241

1.0 mmol of 2-Chloro-benzo[g]quinoxaline, 1.1 mmol of thiol compound and 1.5 mmol of dry sodium acetate are weighed in a round bottom flask containing 15 ml of 1-butanol. The content of the flask is stirred and refluxed for 2 – 4 hours.

(Reactants dissolve in the boiling solvent, and then the products precipitate generally.) Reaction mixture is cooled to 0 – 5°C, and the precipitated crystals are filtered off, washed with water and cold ethanol, the product is dried with suction.

(Compound 234) 2-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.64 min; Mol. Mass: 357
δ (ppm) = 8.90(s, 1H, 3-H), 8.74(s, 1H, 5-H), 8.43(s, 1H, 10-H), 8.21(m, 2H, 6,9-H), 8.05(d, 1H, 6'-H, ^4J = 2.3 Hz), 7.80(d, 1H, 3'-H, ^3J= 8.6 Hz), 7.70(dd, 4'-H), 7.64(m, 2H, 7,8-H).

(Compound 235) 2-(1H-Imidazol-2-yl-sulfanyl)-benzo[g]quinoxaline
Rt: 2.65 min; Mol. Mass: 278
δ (ppm) = 8.72(s, 1H, 3-H), 8.53(s, 1H, 5-H), 8.47(s, 1H, 10-H), 8.22(m, 2H, 6,9-H), 7.65(m, 2H, 7,8-H), 7.57(s, 1H, 3'-H), 7.26(s, 1H, 4'-H).

(Compound 236) 2-(1H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]-quinoxaline
Rt: 2.92 min; Mol. Mass: 279
δ (ppm) = 14.7(b, 1H, NH), 8.82(s, 1H, 3'-H), 8.74(s, 1H, 3-H), 8.72(s, 1H, 5-H), 8.55(s, 1H, 10-H), 8.23(m, 2H, 6,9-H), 7.66(m, 2H, 7,8-H).

(Compound 237) 2-(Pyrimidin-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]quinoxaline
Rt: 3.40 min; Mol. Mass: 372
δ (ppm) = 8.78(s, 1H, 5-H), 8.75(s, 1H, 10-H), 8.57(d, 2H, 3',5'-H, ^3J= 8.5 Hz), 8.24(m, 2H, 6,9-H), 7.78(d, 5"-H, ^3J= 4.7 Hz), 7.67(m, 2H, 7,8-H), 7.33(d, 1H, 3"-H, ^3J= 3.5 Hz), 7.25(t, 1H, 4'-H), 7.12(dd, 1H, 4"-H).

(Compound 238) 2-(1H-Imidazol-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline
Rt: 3.40 min; Mol. Mass: 372
δ (ppm) = 13.41(s, 1H, NH), 8.84(s, 2H, 5,10-H), 8.31(m, 2H, 6,9-H), 7.95(d, 1H, 5"-H, ^3J= 3.8 Hz), 7.89(d, 1H, 2"-H, ^3J= 5.1 Hz), 7.66(m, 2H, 7,8-H), 7.30(t, 1H, 4"-H), 7.13(d, 2H, 2',3'-H, ^3J= 1.8 Hz).

(Compound 239) 2-(2,5-Dichloro-phenylsulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline
Rt: 4.13 min; Mol. Mass: 439

δ (ppm) = 8.71(s, 1H, 5-H), 8.28(s, 2H, 10,6'-H), 8.18(m, 6,9-H), 8.01(m, 2H, 3",5"-H), 7.82(d, 1H, 3'-H, ^{3}J= 8.6 Hz), 7.73(d, 1H, 4'-H), 7.61(m, 2H, 7,8-H), 7.37(dd, 1H, 4"-H, ^{3}J= 3.5 Hz, ^{3}J= 4.7 Hz).

(Compound 240) 2-(Pyrimidin-2-yl-sulfanyl)-benzo[g]quinoxaline

1.0 mmol of 2-Chloro-benzo[g]quinoxaline, 1.1 mmol of thiol compound and 1.5 mmol of dry sodium acetate are weighed in a round bottom flask containing 15 ml of 1-butanol. The content of the flask is stirred and refluxed for 2 – 4 hours. (Reactants dissolve in the boiling solvent, and then the products precipitate generally.) Reaction mixture is cooled to 0 – 5°C, and the precipitated crystals are filtered off, washed with water and cold ethanol, the product is dried with suction.

Rt: 3.15 min; Mol. Mass: 290

δ (ppm) = 9.13(s, 1H, 3-H), 8.81(s, 1H, 5-H), 8.77(s, 1H, 10-H), 8.73(d, 2H, 3'5'-H, ^{3}J= 4.9 Hz), 8.28(m, 2H, 6,9-H), 7.71(m, 2H, 7,8-H), 7.42(t, 1H, 4'-H).

(Compound 241) 4-(3-Chloro-benzo[g]quinoxalin-2-ylsulfanyl)-phenylamine

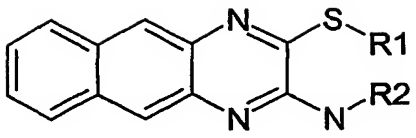
1.0 mmol of 2,3-Dichloro-benzo[g]quinoxaline, 1.1 mmol of 4-aminobenzenethiol compound and 1.5 mmol of dry sodium acetate are weighed in a round bottom flask containing 15 ml of ethanol. The content of the flask is stirred and refluxed for 4 hours. (Reactants dissolve in the boiling solvent, and then the products precipitate generally.) Reaction mixture is cooled to 0 – 5°C, and the precipitated crystals are filtered off, washed with water and cold ethanol, the product is dried with suction. If necessary, purified by chromatography.

Yield: 63%

Rt: 3.53 min; Mol. Mass: 337

δ (ppm) = 8.61(s, 1H, 5-H), 8.36(s, 1H, 10-H), 8.19(m, 2H, 6, 9-H), 7.61(m, 2H, 7, 8-H), 7.27(d, 2H, 2', 6'-H), 6.71(d, 2H, 3', 5'-H, ^{3}J=8.5Hz), 5.68(s, 2H, NH_2)

Example 27



R1,R2=aryl

General Method for the synthesis of Compounds 242-318

A solution of (3-Chloro-benzo[g]quinoxalin-2-yl)-(substituted-phenyl)-amine (0.29mmol), sodium acetate (0.32 mmol) and thiole (0.32 mmol) was refluxed in 8 ml abs. ethanol for 2-6 hours. Reaction mixture was cooled to 0°C, and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

(Compound 242) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

A solution of [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine (0.29 mmol) , sodium acetate (0.32 mmol) and 3,4-dichlorobenzenethiol (0.32 mmol) was refluxed in 8 ml abs. ethanol for 6 hours. Reaction mixture was cooled to 0°C, and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

Yield: 60%

Rt: 4.57 min; Mol. Mass: 588

δ (ppm) ($CDCl_3$) = 8.70(s, 1H, NH), 8.35(s, 1H, 5-H), 8.32(s, 1H, 10-H), 8.00-7.72(m, 6H, 6, 9, 2', 5', 5", 6"-H), 7.58-7.30(m, 5H, 7, 8, 6', 2", 4"-H), 6.19(s, 1H, 2"'-H), 1.41(s, 9H, $-CH_3$)

(Compound 243) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.01min; Mol. Mass: 549

δ (ppm) = 11.10(s, 1H, NH), 8.0-7.0(m, 14H, 5, 6, 7, 8, 9, 10, 3', 5', 6', 7', 2", 3", 4", 5", -H), 6.52(s, 2H, 2'-H), 3.84(s, 3H, $-CH_3$), 1.37(s, 9H, $-CH_3$)

(Compound 244) [5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 3.97min; Mol. Mass: 549

δ (ppm) = 11.1(b, 1H, NH), 8.3-6.8(m, 14H, 5, 6, 7, 8, 9, 10, 3', 5', 6', 7', 2", 4", 5", 6"-H), 6.61(s, 1H, 2'-H), 3.82(s, 3H, $-CH_3$), 1.38(s, 9H, $-CH_3$)

(Compound 245) (3-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.14 min; Mol. Mass: 482

δ (ppm) = 9.74(b, 1H, NH), 8.8-7.6(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 4", 5", 6"-H)

(Compound 246) [3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-chloro-phenyl)-amine

A solution of (3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-phenyl)-amine (0.29 mmol) , sodium acetate (0.32 mmol) and 3-aminobenzenethiol (0.32 mmol) was refluxed in 8 ml abs. ethanol for 4 hours. Reaction mixture was cooled to 0°C, and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

Yield: 77%

Rt: 3.65 min; Mol. Mass: 428

δ (ppm) = 9.50(bs, 1H, NH), 8.8-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 4", 5", 6"-H), 5.86(s, 2H, NH_2)

(Compound 247) (3-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.08 min; Mol. Mass: 441

δ (ppm) = 9.12(bs, 1H, NH), 8.3-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 3', 5', 6', 2", 4", 5", 6"-H), 2.36(s, 3H, $-CH_3$), 2.40(s, 3H, $-CH_3$)

(Compound 248) (3-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 3.79 min; Mol. Mass: 443

δ (ppm) = 9.13(s, 1H, NH), 8.3-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 4", 5", 6"-H), 3.76(s, 3H, $-CH_3$)

(Compound 249) (3-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 3.93 min; Mol. Mass: 448

δ (ppm) = 9.23(b, 1H, NH), 8.3-7.7(m, 8H,.5, 6, 9, 10, 3', 6', 2", 4"-H), 7.7-7.4(m, 5H, 7, 8, 4', 5', 5"-H), 7.17(dd, 1H, 6"-H, ^3J=8.0Hz, ^4J =1.2Hz)

(Compound 250) (3-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 3.85 min; Mol. Mass: 443
δ (ppm) = 9.10(b, 1H, NH), 8.3(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 4", 5", 6"-H), 3.82(s, 3H, $-CH_3$)

(Compound 251) (3-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 3.87 min; Mol. Mass: 431
δ (ppm) = 9.13(b, 1H, NH), 8.3-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 4", 5", 6"-H)

(Compound 252) (3-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.03 min; Mol. Mass: 448
δ (ppm) = 9.16(b, 1H, NH), 8.3-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 6', 2", 4", 5", 6"-H)

(Compound 253) (3-Chloro-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.23 min; Mol. Mass: 482
δ (ppm) = 9.17(b, 1H, NH), 8.3-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 2', 5' 6', 2", 4", 5", 6"-H)

(Compound 254) (3-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 3.87 min; Mol. Mass: 443
δ (ppm) = 9.08(b, 1H, NH), 8.3-7.0(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 4", 5", 6"-H), 3.87(s, 3H, $-CH_3$)

(Compound 255) (3-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
Rt: 3.98 min; Mol. Mass: 427
δ (ppm) = 9.08(bs, 1H, NH), 8.3-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 4", 5", 6"-H)

(Compound 256) [3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

Rt: 4.88 min; Mol. Mass: 516

δ (ppm) = 9.48(b, 1H, NH), 8.3-7.6(m, 11H, 5, 6, 9, 10, 2', 4', 5', 2", 3", 5", 6"-H), 7.50(m, 2H, 7,8-H)

(Compound 257) [3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

Rt: 3.94min; Mol. Mass: 462

δ (ppm) = 9.24(bs, 1H, NH), 8.3-6.7(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H, 5.38(s, 2H, NH_2)

(Compound 258) [3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

A solution of (3-Chloro-benzo[g]quinoxalin-2-yl)-(4-trifluoromethyl-phenyl)-amine (0.29 mmol), sodium acetate (0.32 mmol) and thiole (0.32 mmol) was refluxed in 8 ml abs. ethanol for 4 hours. Reaction mixture was cooled to 0°C, and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

Yield: 60%

Rt: 4.76min; Mol. Mass: 475

δ (ppm) = 9.33(bs, 1H, NH), 8.3-7.7(m, 8H, 5, 6, 9, 10, 2", 3", 5", 6"-H), 7.55(d, 1H, 6'-H, ^3J=7.7Hz), 7.47(m, 2H, 7, 8-H), 7.34(s, 1H, 3'-H), 7.18(d, 1H, 5'-H, ^3J=7.7Hz), 2.40(s, 3H, $-CH_3$), 2.37(s, 3H, $-CH_3$)

(Compound 259) [3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

Rt: 4.20 min; Mol. Mass: 477

δ (ppm) = 9.36(s, 1H, NH), 8.3-7.7(m, 8H, 5, 6, 9, 10, 2", 3", 5", 6"-H), 7.65(d, 1H, 6'-H, ^3J=8.2Hz), 7.59(t, 1H, 4'-H, ^3J=8.2Hz), 7.48(m, 2H, 7, 8-H), 7.26(d, 1H, 3'-H, ^3J=8.2Hz), 7.13(t, 1H, 5'-H, $^3J_{5'4'}=^3J_{5'6'}$8.2Hz), 3.77(s, 3H, $-CH_3$),

(Compound 260) [3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

Rt: 4.44 min; Mol. Mass: 481

δ (ppm) = 9.45(bs, 1H, NH), 8.3-74(m, 14H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 261) [3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.29 min; Mol. Mass: 477
δ (ppm) = 9.32(bs, 1H, NH), 8.3-7.4(m, 11H, 5, 6, 7, 8, 9, 10, 5', 2", 3", 5", 6"-H), 7.30(s, 1H, 2'-H), 7.29(d, 1H, 6'-H, ^{3}J=7.8Hz), 7.14(d, 1H, 4'-H, ^{3}J=7.8Hz), 3.82(s, 3H, -CH_3)

(Compound 262) [3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.33 min; Mol. Mass: 465
δ (ppm) = 9.35(bs, 1H, NH), 8.3-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 3", 5", 6"-H)

(Compound 263) [3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.66 min; Mol. Mass: 481
δ (ppm) = 9.38(bs, 1H, NH), 8.3-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 264) [3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 5.12 min; Mol. Mass: 516
δ (ppm) = 9.38(bs, 1H, NH), 8.3-77(m, 11H, 5, 6, 9, 10, 2', 5', 6', 2", 3", 5", 6"-H), 7.50(m, 2H, 7,8-H)

(Compound 265) [3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.31 min; Mol. Mass: 477
δ (ppm) = 9.29(s, 1H, NH), 8.3-7.7(m, 8H, 5, 6, 9, 10, 2', 3', 5', 6'-H), 7.64(d, 2H, 3", 5"-H, ^{3}J=8.4Hz), 7.48(m, 2H, 7,8-H), 7.15(d, 2H, 2", 6"-H, ^{3}J=8.4Hz), 3.87(s, 3H, -CH_3)

(Compound 266) [3-(3-p-Tolylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.56 min; Mol. Mass: 461
δ (ppm) = 9.31(bs, 1H, NH), 8.3-7.7(m, 8H, 5, 6, 9, 10, 2", 3", 5", 6"-H), 7.7-7.3(m, 6H, 2', 3', 5', 6', 7, 8-H), 2.43(s, 3H, -CH_3)

(Compound 267) [3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
Rt: 4.76 min; Mol. Mass: 526
δ (ppm) = 9.37(bs, 1H, NH), 8.3-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 268) [3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-trifluoromethyl-phenyl)-amine
Rt: 4.73 min; Mol. Mass: 475
δ (ppm) = 9.34(bs, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 3", 5", 6"-H), 2.35(s, 6H, $-CH_3$)

(Compound 269) [3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.58 min; Mol. Mass: 466
δ (ppm) = 9.28(b, 1H, NH), 8.3-7.3(m, 12H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 5", 6"-H), 6.95(m, 1H, 4"-H)

(Compound 270) [3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 3.81 min; Mol. Mass: 412
δ (ppm) = 9.03(bs, 1H, NH), 8.26(s, 1H, 5-H), 8.20(s, 1H, 10-H), 8.1-7.3(m, 7H, 7, 8, 9, 10, 2", 5", 6"-H), 7.18(t, 1H, 5'-H), 6.94(m, 1H, 4"-H), 6.88(s, 1H, 2'-H), 6.81(d, 1H, 6'-H, ^3J=7.8Hz), 6.71(d, 1H, 4'-H, ^3J=7.8Hz), 5.38(s, 2H, NH_2)

(Compound 271) [3-(2,4-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.48 min; Mol. Mass: 425
δ (ppm) = 9.13(bs, 1H, NH), 8.3-7.0(m, 12H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 2", 5", 6"-H), 6.94(t, 1H, 4"-H, $^3J_{4"5"} = {}^3J_{4",F}$=8.6Hz), 2.40(s, 3H, $-CH_3$), 2.36(s, 3H, $-CH_3$)

(Compound 272) [3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.01 min; Mol. Mass: 427

δ (ppm) = 9.14(bs, 1H, NH), 8.26(s, 1H, 5-H), 8.1-7.1(m, 12H, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 5", 6"-H), 6.95(m, 1H, 4"-H), 3.76(s, 3H, $-CH_3$)

(Compound 273) [3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.22 min; Mol. Mass: 431
δ (ppm) = 9.25(b, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 5", 6"-H), 6.95(m, 1H, 4"-H)

(Compound 274) [3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.10 min; Mol. Mass: 427
δ (ppm) = 9.14(b, 1H, NH), 8.3-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 5", 6"-H), 6.94(m, 1H, 4"-H), 3.82(s, 3H, $-CH_3$)

(Compound 275) [3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.14 min; Mol. Mass: 415
δ (ppm) = 9.14(bs, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 5", 6"-H), 6.95(m, 1H, 4"-H)

(Compound 276) [3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.42 min; Mol. Mass: 431
δ (ppm) = 9.19(b, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 5", 6"-H), 6.94(t, 1H, 4"-H, $^3J_{5",4"} = {}^3J_{4",F} = 8.2$Hz)

(Compound 277) [3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.80 min; Mol. Mass: 466
δ (ppm) = 9.19(b, 1H, NH), 8.3-7.3(m, 11H, 5, 6, 7, 8, 9, 10, 2', 5', 6', 2", 5", 6"-H), 6.94(m, 1H, 4"-H)

(Compound 278) [3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
Rt: 4.13 min; Mol. Mass: 427
δ (ppm) = 9.08(b, 1H, NH), 8.3-7.3(m, 11H, 5, 6, 7, 8, 9, 10, 2', 6', 2", 5", 6"-H), 7.14(d, 2H, 3', 5'-H, ^3J=9.1Hz), 6.94(m, 1H, 4"-H)

(Compound 279) (3-Fluorophenyl)-(3-p-toylsulfanyl-benzo[g]quinoxalin-2-yl)-amine

Rt: 4.32 min; Mol. Mass: 411

δ (ppm) = 9.11(b, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 5", 6"-H), 6.94(m, 1H, 4"-H), 2.43(s, 3H, $-CH_3$)

(Compound 280) [3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

Rt: 4.50 min; Mol. Mass: 476

δ (ppm) = 9.17(b, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 5", 6"-H), 6.94(m, 1H, 4"-H)

(Compound 281) [3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

Rt: 4.48 min; Mol. Mass: 425

δ (ppm) = 9.15(bs, 1H, NH), 8.3-6.9(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 6', 2", 4", 5", 6"-H), 2.34(s, 6H, $-CH_3$)

(Compound 282) [3-(2,6-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

Rt: 4.35 min; Mol. Mass: 466

δ (ppm) = 9.36(bs, 1H, NH), 8.3-7.4(m, 11H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 2", 5", 6"-H), 6.96(m, 1H, 4"-H)

(Compound 283) (4-Bromo-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 5.12 min; Mol. Mass: 527

δ (ppm) = 9.23(b, 1H, NH), 8.2-7.4(m, 13H,5, 6, 7, 8, 9, 10, 3', 4', 6', 2", 3", 5", 6"-H)

(Compound 284) (4-Bromo-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.02 min; Mol. Mass: 473

δ (ppm) = 8.99(bs, 1H, NH), 8.3-7.4(m, 10H, 5, 6, 7, 8, 9, 10, 2", 3", 5", 6"-H), 7.18(t, 1H, 5'-H), 6.88(s, 1H, 2'-H), 6.81(d, 1H, 4'-H, ^3J=7.6Hz), 6.71(d, 1H, 6'-H, ^3J=7.6Hz), 5.38(s, 2H, NH_2)

(Compound 285) (4-Bromo-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.96 min; Mol. Mass: 486
δ (ppm) = 9.08(bs, 1H, NH), 8.2-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 3', 5', 6', 2", 3", 5", 6"-H), 2.40(s, 3H, $-CH_3$), 2.36(s, 3H, $-CH_3$)

(Compound 286) (4-Bromo-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.28 min; Mol. Mass: 488
δ (ppm) = 9.10(s, 1H, NH), 8.19(s, 1H, 5-H), 8.01(m, 5H, 6, 9, 10, 3", 5"-H), 7.65-7.43(m, 6H, 7, 8, 2", 6", 4', 6'-H), 7.25(d, 1H, 3'-H, ^3J=6Hz), 7.2(t, 1H, 5'-H, ^3J=7Hz).

(Compound 287) (4-Bromo-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.58 min; Mol. Mass: 492
δ (ppm) = 9.20(b, 1H, NH), 8.3-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 288) (4-Bromo-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.41 min; Mol. Mass: 488
δ (ppm) = 9.06(bs, 1H, NH), 8.2-7.4(m, 11H, 5, 6, 7, 8, 9, 10, 5', 2", 3", 5", 6"-H), 7.30(s, 1H, 2'-H), 7.28(d, 1H, 4'-H, ^3J=8.1Hz), 7.13(d, 1H, 6'-H, ^3J=8.1Hz), 3.82(s, 3H, $-CH_3$)

(Compound 289) (4-Bromo-phenyl)-(3-phenylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
Rt: 4.47 min; Mol. Mass: 457
δ (ppm) = 9.08(b, 1H, NH), 8.2-7.4(m, 15H, 5, 6, 7, 8, 9, 10, 2', 3', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 290) (4-Bromo-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.87 min; Mol. Mass: 492
δ (ppm) = 9.12(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 291) (4-Bromo-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 5.38 min; Mol. Mass: 527
δ (ppm) = 9.13(b, 1H, NH), 8.2-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 2', 5', 6', 2", 3", 5", 6"-H)

(Compound 292) (4-Bromo-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.44 min; Mol. Mass: 488
δ (ppm) = 9.04(s, 1H, NH), 8.2-7.4(m, 12H, 5, 6, 7, 8, 9, 10, 3',5', 2", 3", 5", 6"-H), 7.14(d, 2H, 2', 6'-H, ^3J=8.2Hz), 3.87(s, 3H, -CH_3)

(Compound 293) (4-Bromo-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
Rt: 4.73 min; Mol. Mass: 472
δ (ppm) = 9.05(bs, 1H, NH), 8.2-7.3(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 3", 5", 6"-H), 2.43(bs, 1H, NH)

(Compound 294) (4-Bromo-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.98 min; Mol. Mass: 537
δ (ppm) = 9.12(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 295) (4-Bromo-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.94 min; Mol. Mass: 486
δ (ppm) = 9.09(bs, 1H, NH), 8.2-7.2(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 6', 2", 3", 5", 6"-H), 2.34(s, 6H, -CH_3)

(Compound 296) (4-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.90 min; Mol. Mass: 482
δ (ppm) = 9.24(b, 1H, NH), 8.3-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 6', 2", 3", 5", 6"-H)

(Compound 297) (4-Chloro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 3.87 min; Mol. Mass: 428
δ (ppm) = 8.99(s, 1H, NH), 8.2-7.4(m, 10H, 5, 6, 7, 8, 9, 10, 2", 3", 5", 6"-H), 7.18(t, 1H 5'-H, ^{3}J=7.7Hz), 6.88(s, 1H, 2'-H), 6.81(d, 1H, 4'-H, ^{3}J=7.7Hz), 6.71(d, 1H, 6'-H, ^{3}J=7.7Hz), 5.38(s, 2H, NH_2)

(Compound 298) (4-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.78 min; Mol. Mass: 441
δ (ppm) = 9.10(bs, 1H, NH), 8.2-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 3', 5', 6', 2", 3", 5", 6"-H), 2.40(s, 3H, $-CH_3$), 2.36(s, 3H, $-CH_3$)

(Compound 299) (4-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.19 min; Mol. Mass: 443
δ (ppm) = 9.10(s, 1H, NH), 8.2-7.3(m, 12H, 5, 6, 7, 8, 9, 10, 4', 6', 2", 3", 5", 6"-H), 7.26(d, 1H, 3'-H, ^{3}J=8.2Hz), 7.11(t, 1H, 5'-H, ^{3}J=7.3Hz), 3.76(s, 3H, $-CH_3$)

(Compound 300) (4-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.45 min; Mol. Mass: 448
δ (ppm) = 9.20(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 301) (4-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.29 min; Mol. Mass: 443
δ (ppm) = 9.08(b, 1H, NH), 8.2-7.4(m, 11H, 5, 6, 7, 8, 9, 10, 5', 2", 3", 5", 6"-H), 7.30(s, 1h, 2'-H), 7.13(d, 1H, 4'-H, ^{3}J=7.8Hz), 7.13(d, 1H, 6'-H, ^{3}J=7.8Hz), 3.82(s, 3H, $-CH_3$)

(Compound 302) (4-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.32 min; Mol. Mass: 431
δ (ppm) = 9.10(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 3", 5", 6"-H),

(Compound 303) (4-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.68 min; Mol. Mass: 448
δ (ppm) = 9.13(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 6"-H)

(Compound 304) (4-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.33 min; Mol. Mass: 443
δ (ppm) = 9.05(bs, 1H, NH), 8.2-7.1(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 3", 5",6"-H), 3.87(s, 3H, $-CH_3$)

(Compound 305) (4-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
Rt: 4.57 min; Mol. Mass: 427
δ (ppm) = 9.06(b, 1H, NH), 8.2-7.3(m, 14H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 3", 5", 6"-H), 2.43(s, 3H, $-CH_3$)

(Compound 306) (4-Chloro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.80 min; Mol. Mass: 492
δ (ppm) = 9.12(b, 1H, NH), 8.2-7.4(m, 14H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 3", 5", 5", 6"-H)

(Compound 307) (3-Chloro-4-fluoro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.99 min; Mol. Mass: 500.81
δ (ppm) = 9.29(bs, 1H, NH), 8.4-7.4(m, 12H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 5", 6"-H)

(Compound 308) (3-Chloro-4-fluoro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 3.88 min; Mol. Mass: 446
δ (ppm) = 9.07(bs, 1H, NH), 8.3-7.4(m, 9H, 5, 6, 7, 8, 9, 10, 2", 5", 6"-H), 7.18(t, 1H, 5-H), 6.88(s, 1H, 2'-H), 6.81(d, 1H, 6'-H, ^3J=7.2Hz), 6.71(d, 1H, 4'-H, ^3J=7.2Hz), 5.39(s, 2H, NH_2)

(Compound 309) (3-Chloro-4-fluoro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.84 min; Mol. Mass: 459
δ (ppm) = 9.15(s, 1H, NH), 8.28-7.97(m, 6H, 5, 6, 9, 10, 2", 6'-H), 7.55-7.17(m, 6H, 7, 8, 3', 5', 5", 6"-H), 2.40(s, 3H, $-CH_3$), 2.36(s, 3H, $-CH_3$)

(Compound 310) (3-Chloro-4-fluoro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.22 min; Mol. Mass: 461
δ (ppm) = 9.17(bs, 1H, NH), 8.3-7.1(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 5", 6"-H), 3.76(s, 3H, $-CH_3$)

(Compound 311) (3-Chloro-4-fluoro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.52 min; Mol. Mass: 466
δ (ppm) = 9.26(bs, 1H, NH), 8.3-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 3', 4', 5', 6', 2", 5", 6"-H)

(Compound 312) (3-Chloro-4-fluoro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.33 min; Mol. Mass: 461
δ (ppm) = 9.26(bs, 1H, NH), 8.3-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 5", 6"-H)

(Compound 313) (3-Chloro-4-fluoro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.40 min; Mol. Mass: 449
δ (ppm) = 9.16(b, 1H, NH), 8.3-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 5", 6"-H)

(Compound 314) (3-Chloro-4-fluoro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
Rt: 4.77 min; Mol. Mass: 466
δ (ppm) = 9.18(b, 1H, NH), 8.3-74(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 5", 6"-H)

(Compound 315) (3-Chloro-4-fluoro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.38 min; Mol. Mass: 461

δ (ppm) = 9.11(b, 1H, NH), 8.3-7.8(m, 6H, 5, 6, 9, 10, 2", 6"-H), 7.62(d. 2H, 2', 6'-H, ^{3}J=8.1Hz), 7.46(m, 3H, 5", 7, 8-H), 7.13(d, 2H, 3', 5'-H, ^{3}J=8.1Hz), 3.81(s, 3H, -CH_3)

(Compound 316) (3-Chloro-4-fluoro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.62 min; Mol. Mass: 445

δ (ppm) = 9.13(s, 1H, NH), 8.3-7.3(m, 13H, 5, 6, 7, 8, 9, 10, 2', 3', 5', 6', 2", 5", 6"-H), 2.43(s, 3H, -CH_3)

(Compound 317) (3-Chloro-4-fluoro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.90 min; Mol. Mass: 510

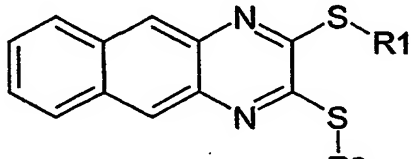
δ (ppm) = 9.18(b, 1H, NH), 8.4-7.4(m, 13H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 6', 2", 5", 6"-H)

(Compound 318) (3-Chloro-4-fluoro-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

Rt: 4.83 min; Mol. Mass: 459

δ (ppm) = 9.17(bs, 1H, NH), 8.3-7.3(m, 12H, 5, 6, 7, 8, 9, 10, 2', 4', 5', 2", 5", 6"-H), 2.34(s, 6H, -CH_3)

Example 28



R1, R2= aryl

General Method for the synthesis of Compounds 319-337

A solution of 0.24 mmol 2,3-dichloro-benzo[g]quinoxaline, 0.5 mmol thiol and 0.5 mmol sodium acetate was refluxed in 5ml abs. ethanol for 4-6 hours. Reaction mixture cooling slowly to 0°C, and the precipitated crystals filtered off, washed with cold ethanol and water, the product dried under vacuum.

(Compound 319) 2,3-Bis-(3-chloro-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.60 min; Mol. Mass: 465
δ (ppm) = 8.30(s, 2H, 5, 10-H), 8.13(m, 2H, 6, 9-H), 7.85(s, 2H, 2'-H), 7.65(m, 6H, 4', 5', 6'-H), 7.56(m, 2H, 7, 8-H)

(Compound 320) 2,3-Bis-(naphthalen-2-yl-sulfanyl)-benzo[g]quinoxaline
Rt: 4.79 min; Mol. Mass: 496
δ (ppm) ($CDCl_3$) = 8.26(s, 2H, 2'-H), 8.12(s, 2H, 5, 10-H), 7.94(m, 6H, 3', 6', 7'-H), 7.85(m, 2H, 6, 9-H), 7.74(d, 2H, 8'-H, ^3J=8.6Hz), 7.60(m, 4H, 4', 5'-H), 7.42(m, 2H, 7, 8-H)

(Compound 321) 2,3-Bis-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.95 min; Mol. Mass: 432
δ (ppm) = 8.16(s, 2H, 5, 10-H), 7.91(m, 2H, 6, 9-H), 7.67(m, 4H, 2', 6'-H), 7.46(m, 2H, 7, 8-H), 7.22(m, 4H, 3', 5'-H)

(Compound 322) 2,3-Bis-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.9 min; Mol. Mass: 456
δ (ppm) = 8.16(s, 2H, 5, 10-H), 7.89(m, 2H, 6, 9-H), 7.61(d, 4H, 2', 6'-H, ^3J=8.5Hz), 7.43(m, 2H, 7, 8-H), 7.05(d, 4H, 3', 5'-H), 3.91(s, 6H' CH_3)

(Compound 323) 2,3-Bis-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 5.30 min; Mol. Mass: 534
δ (ppm) = 8.24(s, 2H, 5, 10-H), 7.96(m, 2H, 6, 9-H), 7.81(d, 2H, 2'-H, ^4J=2.0Hz), 7.59(d, 2H, 5'-H, ^3J=8.3Hz), 7.51(m, 4H, 6', 7, 8-H)

(Compound 324) 2,3-Bis-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.79 min; Mol. Mass: 534
δ (ppm) = 8.24(s, 2H, 5, 10-H), 7.95(m, 2H, 6, 9-H), 7.76(d, 2H, 6'-H, 4_j=2.4Hz), 7.54(d, 2H, 3'-H, ^3J=8.6Hz), 7.49(m, 2H, 7, 8-H), 7.43(dd, 2H, 4'-H)

(Compound 325) 2,3-Bis-(3-bromo-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.64 min; Mol. Mass: 554
δ (ppm) ($CDCl_3$) = 8.22(s, 2H, 5, 10-H), 7.95(m, 2H, 6, 9-H), 7.87(s, 2H, 2'-H), 7.65((d, 4H, 4', 6'-H, ^3J=7.9Hz), 7.48(m, 2H, 7, 8-H), 7.39(t, 2H, 5'-H)

(Compound 326) 2,3-Bis-(4-methyl-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.22 min; Mol. Mass: 424
δ (ppm) = 8.17(s, 2H, 5, 10-H), 7.90(m, 2H, 6, 9-H), 7.58(d, 4H, 2', 6'-H, ^{3}J=8.1Hz), 7.44(m, 2H, 7, 8-H), 7.32(d, 4H, 3', 5'-H), 2.47(s, 6H, -CH_3)

(Compound 327) 2,3-Bis-(3-methyl-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.18 min; Mol. Mass: 424
δ (ppm) = 8.18(s, 2H, 5, 10-H), 7.91(m, 2H, 6, 9-H), 7.52-7.30(m, 10H, 7, 8, 2', 4', 5', 6',-H), 2.45(s, 6H, -CH_3)

(Compound 328) 2,3-Bis-(5-amino-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]quinoxaline
Rt: 2.73 min; Mol. Mass: 408
δ (ppm) = 8.40(s, 2H, 5, 10-H), 8.16(m, 2H, 6, 9-H), 7.58(m, 2H, 7, 8-H), 6.28(s, 4H, NH_2)

(Compound 329) 2,3-Bis--(5-pyridin-4-yl-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]quinoxaline
A solution of 0.24 mmol 2,3-dichloro-benzo[g]quinoxaline, 0.5 mmol 5-(4-pyridyl)-1,3,4-oxadiazole-2-thiol and 0.5 mmol sodiumacetate was refluxed in 5 ml abs. ethanol for 6 hours. Reaction mixture cooling slowly to 0°C , and the precipitated crystals filtered off, washed with cold etanol and water, the product dried under vacuum.
Yield: 64%
Rt: 3.36 min; Mol. Mass: 534
δ (ppm) = 8.85(d, 4H, 2', 6'-H, ^{3}J=6.1Hz), 8.58(s, 2H, 5, 10-H), 8.18(m, 2H, 6, 9-H), 7.98(d, 4H, 3', 5'-H), 7.64(m, 2H, 7, 8-H)

(Compound 330) 2,3-Bis-(5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]quinoxaline
Rt: 2.95min; Mol. Mass: 532
δ (ppm) = 8.74(d, 4H, 2', 6'-H, ^{3}J=6.2Hz), 8.42(s, 2H, 5, 10-H), 8.02(d, 4H, 3', 5'-H), 7.56(m, 2H, 7, 8-H)

(Compound 331) 2,3-Bis-(2-methyl-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.07 min; Mol. Mass: 424
δ (ppm) = 8.17(s, 2H, 5, 10-H), 8.05(m, 2H, 6, 9-H), 7.68(d, 4H, 6'-H, ^{3}J=8.5Hz), 7.49(m, 6H, 7, 8, 3', 4'-H), 7.36(m, 2H, 5'-H), 2.40(s, 6H, -CH_3)

(Compound 332) 2,3-Bis-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.38 min; Mol. Mass: 452
δ (ppm) = 8.20(s, 2H, 5, 10-H), 8.07(m, 2H, 6, 9-H), 7.56(d, 2H, 6'-H, ^{3}J=8.5Hz), 7.51(m, 2H, 7, 8-H), 7.34(s, 2H, 3'-H), 7.18(d, 2H, 5'-H), 2.40(s, 6h, CH_3), 2.35(s, 6H, -CH_3)

(Compound 333) 2,3-Bis-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.89 min; Mol. Mass:456
δ (ppm) = 8.29(s, 2H, 5, 10-H), 8.11(m, 2H, 6, 9-H), 7.55(m, 2H, 7, 8-H), 7.50(t, 2H, 5'-H), 7.32(d, 2H, 2'-H, ^{4}J=2.5Hz), 7.29(d, 2H, 6'-H), 7.15(dd, 2H, 4'-H, ^{3}J=8.3Hz)

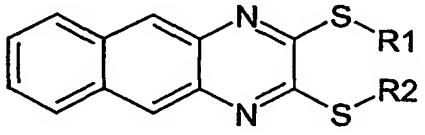
(Compound 334) 2,3-Bis-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 4.39 min; Mol. Mass: 452
δ (ppm) = 8.20(s, 2H, 5, 10-H), 8.08(m, 2H, 6, 9-H), 7.52(m, 4H, 7, 8, 6'-H), 7.40(d, 2H, 3'-H, 3'-H, ^{3}J=8.4Hz), 7.32(d, 2H, 4'-H), 2.34(s, 6H, -CH_3), 2.32(s, 6H, -CH_3)

(Compound 335) 2,3-Bis-(4-amino-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.48min; Mol. Mass: 426
δ (ppm) = 8.22(s, 2H, 5, 10-H), 8.07(m, 2H, 6, 9-H), 7.50(m, 2H, 7, 8-H), 7.28(d, 4H, 2', 6'-H), 6.70(d, 4H, 3', 5'-H, ^{3}J=8.3Hz), 5.64(s, 4H, NH_2)

(Compound 336) 2,3-Bis-(3-amino-phenylsulfanyl)-benzo[g]quinoxaline
Rt: 3.40min; Mol. Mass: 426
δ (ppm) = 8.19(s, 2H, 5, 10-H), 8.02(m, 2H, 6, 9-H), 7.50(m, 2H, 7, 8-H), 7.19(t, 2H, 5'-H, ^{3}J=7.83), 6.86(s, 2H, 2'-H), 6.79(d, 2H, 6'-H), 6.71(d, 2H, 4'-H), 5.66(s, 4H, NH_2)

(Compound 337) 2,3-Bis-(1H-imidazol-2-ylsulfanyl)-benzo[g]quinoxaline
Rt: 2.57 min; Mol. Mass: 376
δ (ppm) = 8.45(s, 2H, NH), 8.20(m, 2H, 6, 9-H), 7.96(s, 4H, 5, 10, 3', 4'-H), 7.64(m, 2H, 7, 8-H)

Example 29



General Method for the synthesis of Compounds 338 - 343
A solution of 4-(3-Chloro-benzo[g]quinoxalin-2-ylsulfanyl)-phenylamine (0.23 mmol) , sodium acetate (0.35 mmol) and thiole (0.27 mmol) was refluxed in 5 ml abs. ethanol for 2-4 hours. Reaction mixture was cooled to 0°C, and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

(Compound 338) 4-[3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
Rt: 3.89min; Mol. Mass: 446
δ (ppm) = 8.27(s, 1H, 5-H), 8.22(s, 1H, 10-H), 8.09(m, 2H, 6, 9-H), 7.83(s, 1H, 2'-H), 7.71-7.60(m, 3H, 4', 5', 6'-H), 7.52(m, 2H, 7, 8-H), 7.30(d, 2H, 2", 6"-H), 6.71(d, 2H, 3", 5"-H, ^3J=8.5Hz), 5.67(s, 2H, NH_2)

(Compound 339) 4-[3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
Rt: 3.70 min; Mol. Mass: 441
δ (ppm) = 8.24(s, 1H, 5-H), 8.21(s, 1H, 10-H), 8.07(m, 2H, 6, 9-H), 7.62(d, 2H, 3', 5'-H, ^3J=8.5Hz), 7.50(m, 2H, 7, 8-H), 7.29(d, 2H, 2", 6"-H, ^3J=8.3Hz), 7.14(d, 2H, 2', 6'-H), 6.71(d, 2H, 3", 5"-H), 5.66(s, 2H, NH_2), 3.87(s, 3H, $-CH_3$)

(Compound 340) 4-[3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
A solution of 4-(3-Chloro-benzo[g]quinoxalin-2-ylsulfanyl)-phenylamine (0.23 mmol) , sodium acetate (0.35 mmol) and 4-fluorobenzenethiol (0.27 mmol) was refluxed in 5 ml abs. ethanol for 4 hours. Reaction mixture was cooled to 0°C,

and the precipitated crystals were filtered off. Washed with cold ethanol and water, dried under vacuum.

Yield: 80%

Rt: 3.72 min; Mol. Mass: 429

δ (ppm) = 8.26(s, 1H, 5-H), 8.20(s, 1H, 10-H), 8.08(m, 2H, 6, 9-H), 7.78(m, 2H, 2', 6'-H), 7.53-7.41(m, 4H, 7, 8, 3', 5'-H), 7.30(d, 2H, 2", 6"-H, ^{3}J=8.3Hz), 6.71(d, 2H, 3", 5"-H), 5.67(s, 2H, NH_2)

(Compound 341) 4-[3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

Rt: 4.10 min; Mol. Mass: 480

δ (ppm) = 8.32(s, 1H, 5-H), 8.27(s, 1H, 10-H), 8.09(m, 2H, 6, 9-H), 8.05(d, 1H, 2'-H, ^{4}J=1.8Hz), 7.85(d, 1H, 5'-H, ^{3}J=8.4Hz), 7.72(dd, 1H, 6'-H), 7.29(d, 2H, 2", 6"-H, ^{3}J=8.3Hz), 6.71(d, 2H, 3", 5"-H), 5.68(s, 2H, NH_2)

(Compound 342) 4-[3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

Rt: 3.97min; Mol. Mass: 480

δ (ppm) = 8.29(s, 1H, 5-H), 8.22(s, 1H, 10-H), 8.09(m, 2H, 6, 9-H), 8.01(d, 1H, 6'-H, ^{4}J=1.5Hz), 7.81(d, 1H, 3'-H, ^{3}J=8.5Hz), 7.72(dd, 1H, 4'-H), 7.53(m, 2H, 7, 8-H), 7.31(d, 2H, 2", 6"-H, ^{3}J=8.3Hz), 6,71(d, 2H, 3', 5'-H), 5.68(s, 2H, NH_2)

(Compound 343) 4-[3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine

Rt: 3.94 min; Mol. Mass: 490

δ (ppm) = 8.27(s, 1H, 5-H), 8.22(s, 1H, 10-H), 8.09(m, 2H, 6, 9-H), 7.95(s, 1H, 2'-H), 7.76(m, 2H, 4', 6'-H), 7.52(m, 3H, 7, 8, 5'-H), 7.30(d, 2H, 2",6"-H, ^{3}J=8.3Hz), 6.71(d, 2H, 3', 5'-H), 5.67(s, 2H, NH_2)

Example 30

(Compound 344) 2-Pyridin-4-yl-4,13-dihydro-14-thia-1,3,3a,5,12-pentaaza-azuleno[5,6-b]anthracene

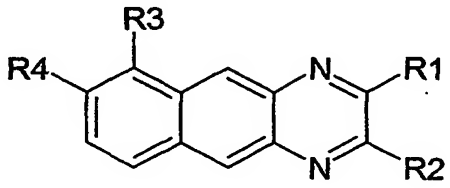
110 mg (0.3 mmol) of 2,3-bis-bromomethyl-1,2-dihydro-benzo[g]quinoxaline, (0.6 mmol) 5-(4-piridyl)-1H-1,2,4-triazol-3-thiol, 50 mg (0.15 mmol) tetrabutyl-ammonium bromide, 3 ml of chloroform and 3 ml 2N aqueous sodium hydroxide

solution were stirring vigorously under argon at ambient temperature for 24 hours. The organic layer was separated, washed with water, dried (Na_2SO_4), filtered and evaporated to dryness. The residue was solidified under methanol. Crystals were collected by filtration and washed methanol to give 32 mg product as a brown powder.

Rt: 2.84 min; Mol. Mass: 382.45

δ (ppm) = 8.82(d, 2H, 2',6'-H, ^{3}J=7.5Hz), 8.68(s, 1H, 5-H), 8.66(s, 1H, 10-H), 8.29(m, 2H, 6,9-H), 7.86(d, 2H, 3',5'-H), 7.69(s, 2H, 7,8-H), 6.08(s, 2H, S-CH_2), 5.09(s, 2H, N-CH_2)

Example 31



R1, R2= H or alkyl or aryl
R3 or R4 alternatively= SO3H, SO2NH2 or H

General Method for the synthesis of Compounds 345-357

Sulfonic acid sodium salt derivative of 2,3-diaminonaphthalene was suspended/dissolved in 2 ml of water and the pH of the solution was adjusted to 7-8 with sodium hydroxide solution. The oxo compound dissolved in 2 ml ethanol and 1 ml DMF was added to the stirred solution. Then the reaction mixture was refluxed for 1 hour then allowed to cool to room temperature. Solvent was removed in vacuum and the residue was triturated with 80% aqueous ethanol, filtrated and dried.

(Compound 345) Benzo[g]quinoxaline-6-sulfonic acid sodium salt

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.69(s, 1H, 5-H), 9.01(s, 1H, OH), 9.00(s, 1H, 5-H), 8.79(s, 1H, 10-H), 8.25(d, 1H, 7-H, ^{3}J=8.6Hz), 8.09(d, 1H, 9-H, ^{3}J=6.3Hz), 7.61(t, 1-H, 8-H)

(Compound 346) 3-(3,4-Dimethoxy-phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.68(s, 1H, 2-H), 9.64(s, 1H, 5-H), 8.76(s, 1H, 10-H), 8.23(d, 1H, 7-H, ^{3}J=8.6 Hz), 8.25(d, 1H, 7-H, ^{3}J=8.5Hz), 8.07(m, 3H, 9,2',5'-H), 7.58(m, 1-H, 8-H), 7.19(m, 1H, 6'-H), 3.96(s, 3H, -CH_3), 3.98(s, 3H, -CH_3)

(Compound 347) 2-Methyl-3-phenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

δ (ppm) = 9.63(s, 1H, 5-H), 8.70(s, 1H, 10-H), 8.19(d, 1H, 9-H, ^{3}J=9.0Hz), 8.04(d, 1H, 7-H, ^{3}J=7.2), 7.84(m, 1H, 8-H), 7.58(m, Ar-H), 2.77(s, 3H, -CH_3)

(Compound 348) 2,3-Diphenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.73(s, 1H, 5-H), 8.22(s, 1H, 10-H), 8.25(d, 1H, 7-H, ^{3}J=8.6Hz), 8.07(d, 1H, 9-H, ^{3}J=6.3 Hz), 7.59(m, 5H, 8,3',5'-H), 7.40(m, 6H, 4',2',6'-H)

(Compound 349) 2,3-Di-p-tolyl -benzo[g]quinoxaline-6-sulfonic acid sodium salt

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.69(s, 1H, 5-H), 8.78(s, 1H, 10-H), 8.23(d, 1H, 7-H, ^{3}J=8.6Hz), 8.07(d, 1H, 9-H, ^{3}J=6.2Hz), 7.59(dd, 1H, 8-H), 7.47(m, 4H, 2',6'-H), 7.20(d, 4-H, 3',5'-H, ^{3}J=7.3 Hz)

(Compound 350) 2,3-Di-furan-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

238 mg (1 mmol) 2,3-Diaminonaphthalene-6-sulfonic acid was dissolved in 2 ml of water and the pH of the solution was adjusted to 7-8 with sodium hydroxide solution. 210 mg (1.1 mmol) 2,2'-furil was dissolved in 2 ml ethanol and 1 ml DMF was added to the stirred solution. Then the reaction mixture was refluxed for 1 hour then allowed to cool to room temperature. Solvent was removed in vacuum and the residue was triturated with 80% aqueous ethanol, filtrated and dried.

Yield: 254 mg (65%)

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.65(s, 1H, 5-H), 8.75(s, 1H, 10-H), 8.21(d, 1H, 7-H, ^{3}J=8.6Hz), 8.06(d, 1H, 9-H, ^{3}J=6.3 Hz), 7.96(s, 1H, 4'-H), 7.93(s, 1H, 4'-H), 7.59(dd, 1H, 8-H), 6.81(m, 4H, 2',3'-H)

(Compound 351) 2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt

δ (ppm) = 9.70(s, 1H, 5-H), 8.81(s, 1H, 10-H), 8.23(d, 1H, 9-H, ^{3}J=8.6Hz), 8.06(d, 1H, 8-H, ^{3}J=6.8Hz), 7.93(s, 1H, 10-H), 7.64-7.49(m, 9H, 8,2',3' 5' 6'-H)

(Compound 352) 2,3-Dithiophen-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt

NMR only, due to its strong adsorption to the column.

δ (ppm) = 9.57(s, 1H, 5-H), 8.70(s, 1H, 10-H), 8.20(d, 1H, 7-H, ^{3}J=8.6 Hz), 8.04(d, 1H, 9-H, ^{3}J=6.3Hz), 7.85(d, 2H, 4'-H, ^{3}J=4.2 Hz), 7.57(t, 1H, 8-H), 7.35(d, 1H, 3'-H, ^{3}J=3.7Hz)

(Compound 353) 2,3-Diphenyl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

δ (ppm) = 7.99(s, 2H, 5,6-H), 7.98(s, 1H, 10-H), 7.66(m, 6H, 8,9,2',6'-H), 7.52(m, 6H, 3',4',5'-H), 7.26(s, 1H, OH)

(Compound 354) 3-(3,5-Bis-trifluoromethyl-phenyl)-benzo[g]quinoxaline-7-sulfonic acid sodium salt

δ (ppm) = 9.88(s, 1H, OH), 9.05(s, 2H, 5,6-H), 8.94(s, 1H, 10-H), 8.84(s, 1H, 4'-H), 8.48(s, 1H, 2'-H), 8.36(s, 1H, 6'-H), 8.24(m, 1H, 9-H), 7.85(m, 1H, 8-H)

(Compound 355) 2,3-Di-thiophen-3-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

δ (ppm) = 8.82(s, 1H, 5-H), 8.73(s, 1H, 6-H), 8.56(s, 1H, OH), 8.45(s, 1H, 10-H), 8.19(d, 1H, 9-H, ^{3}J=8.6Hz), 7.81(d, 1H, 8-H, ^{3}J=6.8Hz), 7.75(s, 1H, 2'-H), 7.72(s, 1H, 2"-H), 7.62(m, 2H, 5',5"-H), 7.28(m, 2H, 4',4"-H)

(Compound 356) 2,3-Di-pyridin-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

δ (ppm) = 9.81(s, 1H, OH), 9.01(s, 2H, 5,6,-H), 8.45(s, 1H, 10-H), 8.29(d, 2H, 6'-H, ^{3}J=6.8Hz), 8.21(d, 1H, 9-H, ^{3}J=8.6Hz), 8.01(d, 2H, 5'-H, ^{3}J=7.7Hz), 7.89(t, 2H, 5'-H), 7.84(d, 1H, 8-H, 7.37(t, 2H, 4'-H)

(Compound 357) 2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt

Example 32

General Method for the synthesis of Compounds 358-360

Sulfonic acid sodium salts were refluxed in thionyl chloride containing a few drops of DMF for 4 hours with stirring. Thionyl chloride was removed in vacuum and the residue was extracted with ice cold ethyl acetate and sodium hydrocarbonate solution. Organic phase was separated dried on sodium sulfate and the solvent was removed in vacuum. The residue was dissolved in isopropanol saturated with ammonia. After standing overnight at room temperature crystals were filtrated off, washed with ether and dried in vacuum.

(Compound 358) 2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-7-sulfon amide

δ (ppm) = 9.49(s, 1H, 5-H), 9.00(s, 1H, 10-H), 8.53(d, 1H, 9-H, ^{3}J=7.2Hz), 8.29(d, 1H, 7-H, ^{3}J=8.2Hz), 7.87(s, 2H, NH_2) 7.76(dd, 1H, 8-H), 7.62(m, 4H, 2',6'-H), 7.27(m, 4H, 3',5'-H)

(Compound 359) 2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-6-sulfonamide

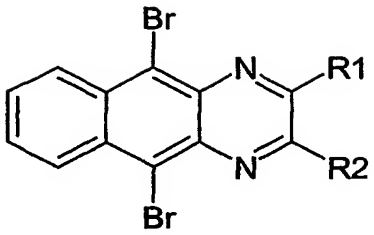
9.50(s, 1H, 5-H), 8.82(s, 1H, 10-H), 8.20(d, 1H, 9-H, ^{3}J=7.8Hz), 8.04(d, 1H, 7-H, ^{3}J=6.8Hz), 7.89(s. 2H, NH_2), 7.85(d, 2H, 5'-H, ^{3}J=4.9Hz), 7.60(dd, 1H, 8-H), 7.27(d, 2H, 3'-H, ^{3}J=3.5Hz), 7.18(dd, 2H, 4'-H)

(Compound 360) 2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline-6-sulfonamide

Rt: 3.37 min; Mol. Mass: 447

δ (ppm) = 9.49(s, 1H, 5-H), 9.00(s, 1H, 10-H), 3.53(d, 1H, 9-H, ^{3}J=7.2Hz), 8.29(d, 1H, 7-H, ^{3}J=8.2Hz), 7.87(s, 2H, NH_2), 7.76(dd, 1H, 8-H), 7.62(m, 4H, 2',6'-H), 7.27(m, 4H, 3',5'-H), 7.62(m, 2H, 5',5"-H), 7.28(m, 2H, 4',4"-H)

Example 33



R1, R2= H or alkyl or aryl

General Method for the synthesis of Compounds 361-377

The suspension of 1,4-dibromo-naphthalene-2,3-diamine and the dioxo reagent in 1.5 ml glacial acetic acid and 1.5 ml ethanol was stirred for 6 hours at reflux temperature. The reaction mixture was cooled to room temperature and the solid precipitate was filtered off, washed with n-hexane and dried.

(Compound 361) 5,10-Dibromo-2-(3-chloro-phenyl)-benzo[g]quinoxaline
Rt: 4.11 min; Mol. Mass: 448
δ (ppm) = 9.86(s, 1H, 2 -H), 8.66(m, 2H, 6,9-H), 8.58(s, 2H, 2`-H), 7.92(m, 2H, 7,8-H), 7.70(m, 3H, 4`,5`,6`-H)

(Compound 362) 2-(3,5-Bis-trifluoromethyl-phenyl)-5,10-dibromo-benzo[g]-quinoxaline
δ (ppm) = 10.04(s, 1H, 2-H), 9.15(s, 2H, 2`,6`-H), 8.69(m, 2H, 6,9-H), 8.44(s, 1H, 4`-H), 7.95(m, 2H, 7,8-H)

(Compound 363) 5,10-Dibromo-2-(3,4-dimethoxy-phenyl)-benzo[g]quinoxaline
Rt: 3.81 min; Mol. Mass: 474
δ (ppm) ($CDCl_3$) = 9.48(s, 1H, 2-H), 8.67(m, 2H, 6,9-H), 8.14(d, 1H, 2`-H, $^4J$=1.8 Hz), 7.89(dd, 1H, 6`-H, ^3J=8.4Hz), 7.73(m, 2H, 7,8-H), 7.05(d, 1H, 5`-H)

(Compound 364) 5,10-Dibromo-2-methyl-3-phenyl)-benzo[g]-quinoxaline
Rt: 3.78 min; Mol. Mass: 428.13
δ (ppm) = 8.54(m, 2H, 6,9-H), 7.90-7.79(m, 4H, 7,8,2`,6`-H), 7.61(m, 3H, 3`,4`,5`-H)

(Compound 365) 5,10-Dibromo-2,3-di-thiophen-2-yl-benzo[g]quinoxaline
Rt: 4.19 min; Mol. Mass: 502
δ (ppm) = 8.60(m, 2H, 6,9-H), 7.67(m, 2H, 7,8-H), 7.59(d, 2H, 5`H, $^3$J=5.0 Hz), 7.53(d, 2H, 3`-H, ^{3}J=3.7 Hz), 7.07(dd, 2H, 4`-H)

(Compound 366) 5,10-Dibromo-2-thiophen-3-yl-3-thiophen-2-yl-benzo [g] – quinoxaline
Rt: 4.14 min; Mol. Mass: 502
δ (ppm) ($CDCl_3$) = 8.64(m, 2H, 6,9-H), 7.93(s, 1H, 2`-H), 7.69(m, 2H, 7,8-H), 7.55(m, 2H, 5`,5``-H), 7.42(m, 1H, 4`-H), 7.21(d, 1H, 3``-H, ^{3}J=3.6 Hz) 7.01(dd, 1H, 4``-H, ^{3}J=4.9 Hz)

(Compound 367) 5,10-Dibromo-2,3-di-thiophen-3-yl-benzo[g]quinoxaline
Rt: 4.13 min; Mol. Mass: 502
δ (ppm) ($CDCl_3$) = 8.66(m, 2H, 6,9-H), 7.79(m, 2H, 2`-H), 7.70(m, 2H, 7,8-H), 7.53(d, 2H, 5`-H, ^{3}J=4.9 Hz), 7.38(m, 2H, 4`-H)

(Compound 368) 5,10-Dibromo-2,3-bis-(5-bromo-2-hydroxy-phenyl)-benzo[g]quinoxaline
Rt: 4.53 min; Mol. Mass: 679
δ (ppm) ($CDCl_3$) = 11.10(s, 2H, OH), 8.53(m, 2H, 6,9-H), 7.68(m, 2H, 7,8-H), 7.64(d, 2H, 6`-H, $^4$J= 2.4 Hz), 7.32(dd, 2H, 5`-H, ^{3}J=8.7 Hz), 6.79(d, 2H, 3`-H)

(Compound 369) 5,10-Dibromo-2,3-di-furan-2-yl-benzo[g]quinoxaline
Rt: 3.82 min; Mol. Mass: 470
δ (ppm) ($CDCl_3$) = 8.64(m, 2H, 6,9-H), 7.69(m, 4H, 7,8,5`-H), 7.03(d, 2H, 3`-H, ^{3}J=3.4 Hz), 6.62(dd, 2H, 4`-H, ^{3}J=7.1 Hz)

(Compound 370) 5,10-Dibromo-2,3-di-pyridin-2-yl- benzo[g]quinoxaline
Rt: 3.57 min; Mol. Mass: 492
δ (ppm) ($CDCl_3$) = 8.72(m, 2H, 6,9-H), 8.40(d, 2H, 6`-H, $^3$J=7.8 Hz), 8.30(d, 2H, 3`-H, ^{3}J=4.6 Hz), 7.94(tt, 2H, 5`-H), 7.74(m, 2H, 7,8-H), 7.28(dd, 2H, 4`-H)

(Compound 371) 5,10-Dibromo-2,3-bis-(3-methoxy-phenyl)-benzo[g]quinoxaline
Rt: 4.03 min; Mol. Mass: 550

δ (ppm) = 8.70(m, 2H, 6,9-H), 7.73(m, 2H, 7,8-H), 7.35(s, 2H, 2`-H), 7.29(m, 4H, 5`,6`-H), 6.99(m, 2H, 4`-H), 3.77(s, 6H, $-CH_3$)

(Compound 372) 5,10-Dibromo-2,3-bis-phenyl-benzo[g]quinoxaline

Rt: 4.11 min; Mol. Mass: 490

δ (ppm) ($CDCl_3$) = 8.69(m, 2H, 6,9-H), 7.72(m, 6H, 7,8,2`,6`-H), 7.42(m, 6H, 3`,4`,5`-H)

(Compound 373) 5,10-Dibromo-2,3-bis-(4-methyl-phenyl)-benzo[g]quinoxaline

Rt: 4.59 min; Mol. Mass: 518

δ (ppm) = 8.68(m, 6,9-H), 7.70(m, 6H, 7,8,2`,6`-H), 7.20(d, 4H, 3`,5-H, ^3J=8.1 Hz), 2.41(s, 6H, $-CH_3$)

(Compound 374) 5,10-Dibromo-2,3-bis-(4-bromo-phenyl)-benzo[g]quinoxaline

Rt: 4.81 min; Mol. Mass: 647

δ (ppm) ($CDCl_3$) = 8.69(m, 2H, 6,9-H), 7.74(m, 2H, 7,8-H), 7.59(m, 4H, 2`,3`,5`,6`-H)

(Compound 375) 5,10-Dibromo-2,3-bis-(4-fluoro-phenyl)-benzo[g]quinoxaline

The suspension of 158 mg (0.5 mmol) 1,4-dibromo-naphthalene-2,3-diamine and 121 mg (0.5 mmol) 4,4'-difluorobenzil in 1.5 ml glacial acetic acid and 1.5 ml ethanol was stirred for 6 hours at reflux temperature. The reaction mixture was cooled to room temperature and the solid precipitate was filtered off, washed with n-hexane and dried.

Yield: 210 mg (80%)

Rt: 4.05 min; Mol. Mass: 526

δ (ppm) = 8.65(m, 2H, 6,9-H), 7.91(m, 2H, 7,8-H), 7.70(m, 4H, 2',6'-H), 7.32(dd, 2H, 3',5'-H, ^3J=8.9 Hz, $^3J_{H,F}$=8.8Hz)

(Compound 376) 5,10-Dibromo-2,3-bis-(4-methoxy-phenyl)-benzo[g]quinoxaline

Rt: 4.11 min; Mol. Mass: 550

δ (ppm) = 8.48(m, 2H, 6,9-H), 7.71(m, 2H, 7,8-H), 7.37(d, 4H, 2`,6`-H ^3J=8.7 Hz), 6.83(d, 4H, 3`,4`-H), 3.79(s, 6H, $-CH_3$)

(Compound 377) {5-[5,10-Dibromo-3-(5-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester

Rt: 3.88 min; Mol. Mass: 646

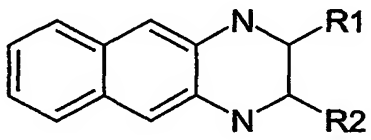
δ (ppm) = 8.56(m, 2H, 6,9-H), 7.85(m, 2H, 7,8-H), 7.39(d, 2H, 3`-H, $^3$J=3.5 Hz), 7.03(d, 2H, 4`-H), 4.10(s, 4H, CH_2), 3.70(s, 6H, -CH_3)

(Compound 378) {5-[5,10-dibromo-3-(4-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester

Rt: 4.19 min; Mol. Mass: 502

δ (ppm) ($CDCl_3$) = 8.63(m, 2H, 6,9-H), 7.69(m, 2H, 7,8-H), 7.57(s, 2H, 5`-H), 7.42(s, 2H, 3`-H), 3.69(m, 10H, CH_2, -CH_3)

Example 34



R1=H,aryl
R2=H, aryl, =O

General Method for the synthesis of Compounds 379-381

1.0 mmol quinoxaline derivative was dissolved in 30 ml acetic acid, and 0.31 g (5.0 mmol) sodium cyanoborohydride was added in small portions to the reaction mixture at room temperature. After stirring for two hours at this temperature the product was filtered off, washed with ether and dried.

(Compound 379) 2,3-Di-thiophen-2-yl-1,2,3,4-tetrahydro-benzo[g]quinoxaline

Rt: 3.34 min; Mol. Mass: 348

δ (ppm) = 7.41(m, 2H, 6,9-H), 7.30(m, 2H, 5`-H), 7.03(m, 2H, 7,8-H), 6.87 (m, 6H, 5-,10-,3`-4`-H), 6.72(s, 2H, NH), 5.04(s, 2H, 2,3-H)

(Compound 380) 3-(5-{3-[5-(2-Carboxy-ethyl)-thiophen-2-yl]-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl}-thiophen-2-yl)-propionic acid

Rt: 3.15 min; Mol. Mass: 493

δ (ppm) = 8.05(s, 2H, 5-,10-H), 7.99-7.68(m, 4H, 6-,9-,3`-H), 7.70(bs, 1H, NH), 7.50(m, 2H, 7,8-H), 7.32-7.21(m, 3H, 4`-H, NH), 6.82(bs, 1H, 2-H), 6.81(m, 1H, 3-H), 2.39(m, 8H, -CH_2-)

(Compound 381) 12687 3-Thiophen-2-yl-3,4-dihydro-1H-benzo[g]quinoxalin-2-one

Rt: 3.04 min; Mol. Mass: 280

δ (ppm) = 10.86(s, 1H, 1-H), 7.59(m, 2H, 6,9-H), 7.38(dd, 1H, 5`-H, $^3$J=4.5 Hz, $^4$J=1.0 Hz), 7.24-7.12(m, 5H, 7-,8,-5-,10-, NH), 6.98(dd, 1H, 3`-H, ^{3}J=3.4 Hz), 6.93 (m, 1H, 4`-H), 5.24(s, 1H, 3-H)

Example 35

General Method for the synthesis of Compounds 382-383

1.0 mmol quinoxaline derivative was dissolved in 30 ml acetic acid, and 0.31 g (5.0 mmol) sodium cyanoborohydride was added in small portions to the reaction mixture at room temperature. After stirring for two hours at this temperature the acetic acid was removed under vacuum. The residue was stirred for half an hour with 50 ml water, and the product was filtered off, washed with water, then ether and dried.

(Compound 382) {5-[3-(5-Carboxymethyl-thiophen-2-yl)-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid

Rt: 3.09 min; Mol. Mass: 465

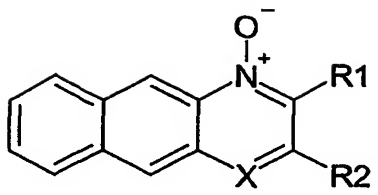
δ (ppm) = 12.50(b, 2H, OH), 7.40(m, 2H, 6-,9-H), 7.03(m, 2H, 7-,8-H), 6.86 (s, 2H, 5-,10-H), 6.69(s, 6H, 3`-,4`-,NH), 4.94 (s, 2H, 2-,3-H), 3.65(s, 4H, -CH_2-)

(Compound 383) 3,4-Dihydro-1H-benzo[g]quinoxalin-2-one

Rt: 2.75 min; Mol. Mass: 198

δ (ppm) = 10.64(s, 1H, 1-H), 7.55(m, 2H, 6-,9-H), 7.16(m, 2H, 7-,8-H), 7.12(s, 1H, 5-H), 6.96 (s,1H, 10-H), 6.37(bs, 1H, NH), 3.82(s, 2H, 3-H)

Example 36



R1,R2= aryl
X= NH, N^+O^-

(Compound 384) 2-(3,5-bis-(trifluoromethyl)-phenyl)-benzo[g]quinoxaline-N-oxide

2-(3,5-Bis-(trifluoromethyl)-phenyl)-benzo[g]quinoxaline (0.2 g, 0.54 mmol) was stirred with 1M peracetic acid (10 ml) at 60°C for 5 hours. The mixture was cooled and the crystal of the product was filtered, washed with diethylether and dried.

Yield: 110 mg (53%)

δ (ppm) = 8.24(s, 2H, 4`-H), 8.48(s, 1H, 2`-H), 8.36(s, 2H, 2,6`-H), 8.08(s, 2H, 5,10-H), 7.96(m, 2H, 6,9-H), 7.55(m, 2H, 7,8-H)

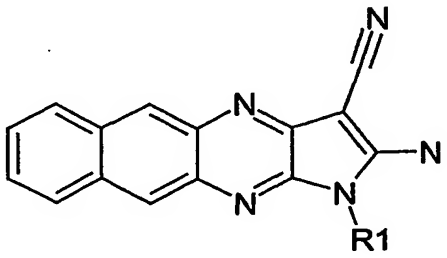
(Compound 385) 2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline 1,4-dioxide

2,3-Bis-(4-fluorophenyl)-benzo[g]quinoxaline (0.66 g, 1.79 mmol) was stirred with 2M peracetic acid (10 ml) at 60°C for overnight. The mixture was cooled and the crystal of the product was filtered, washed with diethylether and dried.

Yield: 300 mg (42%)

Rt: 3.08 min; Mol. Mass: 400

Example 37



General Method for the synthesis of Compounds 386-395

140 mg (0.5 mmol) 2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malononitrile and 1.0 mmol of appropriate amines were refluxed in 3 ml i-propanol for 3-6 hours. The precipitated products were filtrated and washed with diethylether or hexane.

(Compound 386) 2-Amino-1-(2-thiophen-2-yl-ethyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile

Rt: 3.22 min; Mol. Mass: 369

δ (ppm) = 8.05(s, 2H, 5,10-H), 7.79(m, 2H, 6,9-H), 7.73(bs, 2H, 5``-H), 7.30(m, 2H, 7,8-H), 7.28-7.18(m, 4H, 3``,4``-H), 6.80(bs, 2H, NH_2), 3.28(m, 2H, 1`-$H_2$), 2.84(m, 2H, 2`-H_2)

(Compound 387) 2-Amino-1-(2-hydroxy-ethyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile

Rt: 2.84 min; Mol. Mass: 303

δ (ppm) = 8.43(s, 1H, 5-H), 8.42(s, 1H, 10-H), 8.07(m, 2H, 6,9-H), 7.49(m, 2H, 7,8-H), 7.44(b, 3H, OH, NH_2), 4.28(m, 2H, 1'-H_2), 3.76(m, 2H, 2'-H_2)

(Compound 388) 2-Amino-1-(3-methyl-butyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile

Rt: 3.28 min; Mol. Mass: 329

δ (ppm) = 8.77(bs, 2H, NH_2), 8.46(s, 1H, 5-H), 8.43(s, 1H, 10-H), 8.09(m, 2H, 6,9-H), 7.49(m, 2H, 7,8-H), 4.19(bs, 2H, 1'-H_2), 1.60(m, 3H, 2'-H_2, 4'-H), 0.97(bs, 6H, -CH_3)

(Compound 389) 2-Amino-1-(2-hydroxy-propyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile

Rt: 2.86 min; Mol. Mass: 317

δ (ppm) = 8.46(s, 1H, 5-H), 8.41(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.48(m, 2H, 7,8-H), 7.4(b, 2H, NH_2), 4.38(bs, 1H, OH), 4.23(m, 2H, 3'H_2), 3.50(m, 2H, 1'-H_2), 1.88(m, 2H, 2'-H_2)

(Compound 390) 2-Amino-1-[2-(3-fluoro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile

Rt: 3.28 min; Mol. Mass: 381

δ (ppm) = 8.67(bs, 2H, NH_2), 8.45(s, 1H, 5-H), 8.41(s, 1H, 10-H), 8.07(m, 2H, 6,9-H), 7.48(m, 2H, 7,8-H), 7.34-6.97(m, 4H, 2",4",5",6"-H), 4.42(m, 2H, 1'-H_2), 3.08(m, 2H, 2"-H_2)

(Compound 391) 2-Amino-1-[2-(3-chloro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile
Rt: 3.35 min; Mol. Mass: 397
δ (ppm) = 8.75(bs, 2H, NH_2), 8.45(s, 1H, 5-H), 8.41(s, 1H, 10-H), 8.20(m, 2H, 6,9-H), 7.48(m, 3H, 7,8,2"-H), 7.27(m, 3H, 4",5",6"-H), 4.43(m, 2H, 1'-H_2), 3.06(m, 2H, 2'-H_2)

(Compound 392) 2-Amino-1-[2-(4-methoxy-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile
Rt: 3.22 min; Mol. Mass: 393
δ (ppm) = 8.51(bs, 2H, NH_2), 8.45(s, 1H, 5-H), 8.39(s, 1H, 10-H), 8.07(m, 2H, 6,9-H), 7.48(m, 2H, 7,8-H), 7.23(d, 2H, 3",5"-H, ^{3}J=8,5H2), 6.84(d, 2H, 2",6"-H), 4.35(m, 2H, 1'-H_2), 2.97(m, 2H, 2'-H_2)

(Compound 393) 2-Amino-1-(2-cyclohex-1-enyl-ethyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile
Rt: 3.38; Mol. Mass: 367
δ (ppm) = 8.76(bs, 2H, NH_2), 8.44(s, 1H, 5-H), 8.42(s, 1H, 10-H), 8.08(m, 2H, 6,9-H), 7.48(m, 2H, 7,8-H), 5.16(s, 1H, 2"-H), 4.30(bs, 2H, 1'-H_2), 2.32(bs, 2H, 2'-H_2), 2.09, 1.63, 1.44, 1.25(bs, 8H, 3",4",5",6"-H_2)

(Compound 394) 2-Amino-1-(3-imidazol-1-yl-propyl)-1H-benzo[g]pyrrolo-[2,3-b]quinoxaline-3-carbonitrile
Rt: 2.60 ; Mol. Mass: 367
δ (ppm) = 8.40(s, 2H, 5,10-H), 8.3(bs, 2H, NH_2), 8.07(m, 2H, 6,9-H), 7.69(s, 1H, 2"-H), 7.48(m, 2H, 7,8-H), 7.26(s, 1H, H, 4"-H), 6.90(s, 1H, 5"-H), 4.20(m, 2H, 1'-H_2), 4.09(m, 2H, 3'-H_2), 2.18(m, 2H, 2'-H_2)

(Compound 395) 1-(2-Hydroxy-ethyl)-2-oxo-2,3-dihydro-1H-benzo[g]pyrrolo[2,3-b]quinoxaline-3-carboxylic acid ethyl ester
The product was obtained from 185 mg (0.5 mmol) 2-(3-chloro-benzo[g]quinoxalin-2-yl)-malonic acid diethyl ester and 61 mg (1.0 mmol) 2-amino-ethanol according to the General Method for compounds 386 - 395.
Yield: 84 mg (45%)
Rt: 2.94 min; Mol. Mass: 351

δ (ppm) = 8.31(s, 1H, 5-H), 8.19(s, 1H, 10-H), 7.96(m, 2H, 6,9-H), 7.38(m, 2H, 7,8-H), 4.97(bs, 1H, OH), 4.22(q, 2H, O-CH_2), 3.94(m, 2H, 2'-H_2), 3.66(m, 2H, 1`-H2), 1.29(t, 3H, -CH_3)

Example 38

(Compound 396) 2-(2,3-Dihydro-1-oxa-4,5,12-triaza-naphthacen-4-yl)-ethanol

2,3-Dichloro-benzo[g]quinoxaline (0.32 mmol) and the appropriate aromatic amine (1.28 mmol) was heated overnight in 15 ml of isopropyl alcohol. The solution was enhanced by adding a few drops of DMF if necessary. After cooling, the precipitated crystals were filtered off, washed with propanol and dried under vacuum.

Rt: 2.87 min; Mol. Mass: 281

δ (ppm) = 7.89(s, 2H, 5,10-H), 7.76(m, 2H, 6,9,-H), 7.35(m, 2H, 7,8-H), 5.03(bs, 1H, OH), 3.98(m, 2H, O-CH_2), 3.68(m, 4H, 2`-H_2), 3.28(m, 4H, N-CH_2)

Example 39

(Compound 397) 2-[2-(2,4-Dichlorophenyl)-vinyl]-3-thiophen-2-yl-benzo[g]quinoxaline

110 mg (0.4 mmol) 2-Methyl-3-thiophen-2-yl-benzo[g]quinoxaline and 70 mg 2,4-dichlorobenazaldehyde was refluxed in 2 ml acetic anhydride for 4 hours. The solvent was evaporated under reduced pressure. The residue was solidified under methanol. Crystals were collected by filtration, washed with water, methanol and ether yielded 70 mg product as a brown powder.

Rt: 4.30 min; Mol. Mass: 433

δ (ppm) = 8.80(s, 1H, 5-H), 8.71(s, 1H, 10-H), 8.27(m, 3H, 6,9,3"-H),7.99(m, 3H, 5',6",vinyl-1-H), 7.77(m, 2H, 3',5"-H), 7.63(m, 2H, 7,8-H), 7.52(d, 1H, vinyl-2-H, ^3J=9.1Hz), 7.32(m, 1H, 4'-H)

Example 40

(Compound 398) 1,2,3,4-Tetrahydrobenzo[b]phenazine

158 mg (1 mmol) 2,3-Diaminonaphthalene was dissolved in the mixture of 1 ml DMF and 3 ml ethanol with gentle warming. After dissolving of the amine it was cooled to room temperature and the solution of 123 mg (1.1 mmol) 1,2-cyclohexanedione in 1 ml ethanol was added with stirring. The reaction mixture was refluxed for 1 hour then allowed to cool to room temperature while the

product crystallized. Crystals were collected by filtration, washed with ether and dried in vacuum.

Yield: 200 mg (84%)

Rt: 3.25 min; Mol. Mass: 234.30

δ (ppm) = 8.59(s, 2H, 5,10-H), 8.18(m, 2H, 6,9-H), 7.59(m, 2H, 7,8-H), 3.32(s, 4H, 2',5'-H), 1.99(s, 4H, 3',4'-H)

Example 41

(Compound 399) 2-(5-Pyridin-4-yl-1H-[1,2,4]triazole-3-ylsulfanyl)-benzo[g]quinoxaline

The compound was obtained from 140 mg (0.653 mmol) of 2-chloro-benzo[g]quinoxaline and 128 mg (0.718 mmol) of 5-pyridin-4-yl-1H-[1,2,4]triazole-3-thiol according to the General Method for compounds 234 – 241.

Rt: 2.95 min; Mol. Mass: 356.41

δ (ppm) = 8.89(s, 1H, 3-H), 8.76(s, 2H, 5-H, NH), 8.56(s, 1H, 10-H), 8.23(m, 2H, 6,9-H), 7.98(d, 2',6'-H, ^3J = 8.8Hz), 7.65(m, 4H, 7,8,3',5'-H)

(Compound 400) 2-(1H-Benzoimidazole-2-ylsulfanyl)-benzo[g]-quinoxaline

The compound was obtained from 140 mg (0.653 mmol) of 2-chloro-benzo[g]quinoxaline and 108 mg (0.718 mmol) of 1H-benzoimidazole-2-thiol according to the General Method for compounds 234 – 241.

Rt: 3.19 min; Mol. Mass: 328.40

δ (ppm) = 13.3(s, 1H, NH), 8.88(s, 1H, 3-H), 8.76(s, 1H, 5-H), 8.72(s, 1H, 10-H), 8.25(m, 2H, 6,9-H), 7.67(m, 4H, 7,8,5',6'-H), 7.29(m, 2H, 4',7'-H)

Example 42

Compounds 401 – 406 were synthesized according to the General Method for preparing compounds 13 – 30.

(Compound 401) 2-(4-Nitrophenyl)-benzo[g]quinoxaline

9.73(s, 1H, 2-H), 8.88(s, 1H, 5-H), 8.84(s, 1H, 10-H), 8.67(d, 2H, 3',5'-H, ^3J=8.9Hz), 8.46(d, 2H, 2',6'H), 8.29(m, 2H, 6,9-H), 7.69(m, 2H, 7,8-H)

(Compound 402) 2,3-Dimethyl-benzo[g]quinoxaline

8.58(s, 2H, 5,10-H), 8.18(m, 2H, 6,9-H), 7.59(m, 2H, 7,8-H), 2.72(s, 6H, CH_3)

(Compound 403) 2-Phenyl-3-trifluoromethyl-benzo[g]quinoxaline
9.06(s, 1H, 5-H), 8.93(s, 1H, 10-H), 8.34(m, 2H, 6,9-H), 7.78(m, 2H, 7,8-H), 7.69(m, 2H, 2',6'-H), 7.57(m, 3H, 3',4',5'-H)

(Compound 404) 2-Methyl-3-phenyl-benzo[g]quinoxaline
8.74(s, 1H, 5-H), 8.70(s, 1H, 10-H), 8.22(m, 2H, 6,9-H), 7.79(m, 2H, 2',6'-H), 7.66-7.56(m, 5H, 7,8,3',4',5'-H), 2.74(s, 3H, CH_3)

(Compound 405) 2,3-Bis-(4-bromophenyl)-benzo[g]quinoxaline
8.85(s, 2H, 5,10-H), 8.28(m, 2H, 6,9-H), 7.67(m, 2H, 7,8-H), 7.64(d, 4H, 2',6'-H, ^3J=8.5Hz, 7.50(d, 4H, 3',5'-H)

(Compound 406) 2-(4-Fluorophenyl)-benzo[g]quinoxaline
10.21(bs, 1H, NH), 8.63(s, 1H, 2-H), 8.48(s, 1H, 5-H), 8.25(s, 1H, 10-H), 8.09(m, 2H, 6,9-H), 7.50(m, 2H, 7,8-H), 7.26(t, 2H, 3',5'-H, $^3J_{H,H}=^3J_{H,F}$=8.6Hz), 6.84(m, 2H, 2',6'-H)

Example 43: Mycobacteria

Materials and methods

Bacterial strains and culture conditions

M. tuberculosis ($H_{37}Rv$), *M. bovis* BCG (Copenhagen) and *E. coli* (XL-1 blue and BL-21) were used for the generation of lysates and for growth assays. Mycobacteria were grown in Middlebrook 7H9 medium (Difco) supplemented with 10 % Middlebrook OADC enrichment (Difco), 0.05 % Tween-80 and 0.5 % glycerol. *E. coli* was cultivated in LB- or TB-broth media without any additional ingredients.

GST-fusion protein purification

Purification of GST-fusion proteins was in principle done as described in (Smith,D.B. and Corcoran, L. M., in Current Protocols in Molecular Biology Vol.2, 1990). *E. coli* BL 21 cultures containing the respective plasmids were grown overnight in TB-broth medium. After IPTG (Isopropylthiogalactoside) induction, the suspensions were incubated additional 16 h at room temperature. The bacteria were harvested by centrifugation, resuspended in PBS (Phosphate buffer saline) and lysed by sonification. After addition of Triton X-100 (1 % end concentration) and subsequent clarifying of the lysates the GST-fusion protein was purified by addition of GST-sepharose following PBS washes. The proteins were eluted with elution buffer containing 50mM glutathion, 20mM Tris (pH 8.0.), 0.1 M NaCl, 0.1 M Triton X-100 and 1 mM DTT (Dithiothreitol). Subsequently, the eluates were dialyzed in 20 mM HEPES (pH 7.5), 30 % glycerol.

Determination of protein kinase activity

The activity of all Pkns was determined by addition of myelin basic protein as external substrate. The buffer conditions were: 20 mM HEPES (pH 7.5), 20 mM $MgCl_2$ and 5 mM $MnCl_2$ for all kinases except PknG, I,J and L. These protein kinases required lower salt conditions (1 mM $MgCl_2$ and 1 mM $MnCl_2$). The optimal ATP (adenosine triphosphate) concentration for each kinase was determined by titration of ATP (from 0.0033 µM to 100 µM). The inhibitor studies were performed with ATP concentrations similar to the K_m for ATP.

Growth Assays for *M. tuberculosis*, *M. bovis* BCG and *E. coli*

The growth assays were performed as described in Yajko DM, Madej JJ, Lancaster MV, Sanders CA, Cawthon VL, Gee B, Babst A, Hadley WK.

Colorimetric method for determining MICs of antimicrobial agents for Mycobacterium tuberculosis. J Clin Microbiol. 1995 Sep;33(9):2324-7 and Franzblau SG, Witzig RS, McLaughlin JC, Torres P, Madico G, Hernandez A, Degnan MT, Cook MB, Quenzer VK, Ferguson RM, Gilman RH. Rapid, low-technology MIC determination with clinical Mycobacterium tuberculosis isolates by using the microplate Alamar Blue™ assay. J Clin Microbiol. 1998 Feb;36(2):362-6.

Bacteria were seeded to 96-well plates containing the respective inhibitors. After addition of Alamar Blue™, the ratio of extinction at 570/610nm wavelength or the fluorescence (560/590 nm) was measured. The bacteria-containing plates were incubated at 37 °C for three days. After incubation time, the absorption at 570/610nm wavelength was determined.

E. coli growth was assayed by the measurement of the optical density at 610 nm wavelength.

Example 44: HCMV

RICK Kinase-Assay on Basic-Flashplates

The effect of the inventive compounds according to formula (I) on the activity of RICK kinase was evaluated in *in vitro* kinase assays.

RICK enzyme was isolated form HEK 293 cells infected with Adeno virus containing the RICK coding region. The adenovirus used here were all E1, E3 defective derivatives of adenovirus type 5 (W.C. Russell, J. Gen. Virol. 2000, 81, 2573-2604). The coding region for RICK (Acc No AF027706) was amplified by PCR using an upstream primer containing an *Hind*III recognition site and a downstream primer containing an XbaI site but without stop-codon to allow expression of fusion proteins with a Strep-tag (Skerra, A. and Schmidt, T. G., Methods Enzymol. 2000;326:271-304). The cDNA coding for human RICK was cloned into the transfer plasmid (pPM7) between the CMV (cytomegalo virus) immediately early promoter/enhancer and the rabbit beta-globin intron/polyadenylation signal. This expression cassette was inserted into a bacterial plasmid borne-adenovirus genome using recombination in bacteria (C. Chartier et al., J. Virol. 1996, 70, 4805-4810). A cloned version of the novel genome was identified, the viral genome was released from the plasmid by

restriction enzyme digestion and virus replication was initiated by transfecting the genome into HEK 293 cells using a modified PEI transfection method (A.-I. Michou et al., J. Virol. 1999, 73, 1399-1410). Virus was amplified in modified HEK 293 cells (F.L. Graham et al., J. Gen. Virol. 1977, 36, 59-74) and purified from cell lysates using streptavidin columns (M. Cotten et al., Adenovirus polylysine DNA conjugates. In Current Protocols in Human Genetics; John Wiley and Sons, Inc. New York. 1996 pp. 12.3.1-12.3.33; Skerra, A. and Schmidt, T. G., Methods Enzymol. 2000;326:271-304.).

The RICK kinase reaction took place in a total volume of 60 µl in basic flash plates. Following the addition of 20 µl basic buffer (50 mM Hepes pH 7.5, 1 mM $MgCl_2$, 1 mM $MnCl_2$), 20 µl assay buffer (4.5 µM ATP, 60 ng/µl Histone 2B) and 0.5 µCi $\gamma[^{33}P]$ATP, various concentrations of benzo[g]quinoxaline compounds were given to the reaction mix. The reaction was started by the addition of 2 µl RICK enzyme diluted in basic buffer. After incubation for 1 hr at room temperature the reaction was stopped by adding 20 µl 0.5 M EDTA. The incubate in the flash plates was continued for 2 hrs to allow binding of histone to the wells. The wells were wash each 3x with 200 µl 0.5M EDTA and incorporated radioactivity measured in a Microbeta reader (Wallac). As negative control 20 µl 0.5 M EDTA was added to the well before addition of RICK enzyme.

UL97 Kinase-Assay on Immobilon Plate

The effect of selected benzo[g]quinoxaline compounds were tested on a the viral kinase UL-97. This kinase is derived from human cytomegalovirus (HCMV). (Marschall et al., J Gen Virol. 82, 2001, 1439-1450; Marschall et al., J Gen Virol. 83, 2002, 1013-1023). The UL-97 gene was cloned into a baculovirus vector on order to produce GST (glutathione S-transferase) fusion protein. Insect cells (Sf9) were infected and GST-UL-97 purified via glutathione affinity columns according to standard procedures.

UL-97 Kinase Reaction:

The UL-97 kinase reaction was performed as described (Marschall et al., J Gen Virol. 82, 2001, 1439-1450). Briefly, 10 µl Assay buffer (3 µM ATP, 60µg/ml myelin basic protein (MBP) as substrate), 1,0 µCi γ-$[^{33}P]$ATP and 10 µl Basic buffer (20mM Tris-HCl 7.5, 500 µM $MnCl_2$, 1mM DTT) (DTT: dithiothreitol) were given to the test tube before adding various concentrations of benzo[g]quinoxaline compounds. The reaction was started by adding 0.2 µl UL97 kinase, purified from infected Sf9-insect cells as described above. The

total volume was adjusted with Basic buffer to a final volume of 30 µl. The reaction mix was incubated for 1 hr at 30°C. For negative control, 10 µl 0.1M EDTA (ethylene diamine tetraacetate) was added to reaction mix before addition of UL-97 protein kinase. The reaction was stopped by addition of 10 µl 0.1 M EDTA.

Measuring Incorporation of Radioactivity:
The Immobilon plate (Millipore) was rinsed with 50 µl methanol/well. Following addition of 100 µl 0.1 M EDTA, 20 µl of each kinase reaction mix was added to one well of the Immobilon plate. Each well was washed 4x with 250 µl 0.75% phosphoric acid and 1x with 50 µl methanol. After addition of 50 µl scintillation cocktail (Roth, Germany) per well incorporation of radioactivity was measured using a Betareader (Wallac) and enzymatic activity calculated.

Example 45: HBV

Effect of selected benzo[g]quinoxaline compounds in amounts of replication-competent cytoplasmic capsids in the HepG2-2.2.15 cell culture system.

HepG2-2.2.15 human hepatoma cells, obtainable according to the procedure described in Sells et al., 1987, Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 1005-1009, which is fully incorporated by reference, were plated in 12-well cell culture dishes in DMEM medium supplemented with fetal bovine serum. After incubation at 37°C in a humidified, 5% CO_2 environment for 16-24 hours, the monolayer of HepG2-2.2.15 cells was washed and the medium was replaced with complete medium containing 20 µM of test compound. Toxicity of the compounds was determined by microscopic observation. Three days following administration of the test compound, cells were lysed with 500 µl NP-40 lysis buffer (150 mM NaCl, 10 mM Tris-HCl pH 7.5, 0.5% NP-40, 0.5 mM PMSF) (PMSF: phenylmethylsulfonyl fluoride). Cellular debris and nuclei were removed by centrifugation at 13000 rpm, 4°C for 10 minutes, and the resulting supernatant was used to isolate cytoplasmic HBV capsids by immunoprecipitation with an anti- HBV-core antigen antibody (DAKO Diagnostika GmbH, B0586). Immunoprecipitated cores were incubated in 45 µl of EPR-buffer (50 mM Tris-HCl pH7.5; 50 mM NH_4Cl, 40 mM MgCl, 0.3% 2-Mercaptoethanol, 1% NP40) with a mixture of dATP, dGTP and dTTP (110 µM each) and 10 µCi of ^{32}P-dCTP (6000 Ci/mmol; Amersham-Pharmacia) for 3 h at 37°C. The reaction was chased with 110µM of cold dCTP for 30 min at 37°C,

and terminated with 5 µl of 10% SDS. Proteins were digested by proteinase K treatment. After removing free nucleotides with microspinG50 columns (Amersham-Pharmacia), the HBV-DNA was ethanol-precipitated in the presence of carrier. The DNA products were separated by vertical agarose-gel electrophoresis and visualized by autoradiography. Quantification was done with a Fuji phospoimager.

Example 46: Diabetes

Assays are conducted according to the General Kinase Assay Protocol given in example 52.

Example 47: Inhibition of T-tropic and M-tropic HIV-1

Materials and Methods:

Jurkat cells (species : human T-cell leukaemia; special characteristics: cells are permissive for growth of T-cell tropi viruses; source: Hauber Lab) or PM1 cells (species: clonal derivative of HUT 78; special characteristics: cells are permissive for growth of macrophage and T-cell tropic viruses; source: Dr. Marvin Reitz, courtesy of the NIH AIDS Research and Reference Reagent Program) were stimulated with Phytohemagglutinin (PHA-P, Product No. L9132 from Sigma, Saint Louis, Missouri, USA) in a concentration of 2 µg/ml ($1.5x10^6$ cells/ml) and Hexadimethrine Bromide (Polybrene, Product No. H9268 from Sigma) in a concentration of 2 µg/ml ($1.5x10^6$ cells/ml) in RPMI 1640 medium containing 10% fetal calf serum (FCS, Pansystems GmbH, Aidenbach, Germany) and antibiotics for 3 days.

For HIV-1 infection, $5x10^7$ cells were resuspended in 500µl culture medium without drugs and incubated in a 50 ml blue-cap-tube at 37°C for 5 hrs with HIV-1 high titer viral stocks. Jurkat cells were infected with the T-cell tropi strain HIV-1 NL4-3, PM! Cells with the macrophage tropic strain HIV-1 Ba-L (both from the NIH AIDS research and Reference Reagent Program). After infection, cells were washed twice with PBS without Ca^{2+} and Mg^{2+} to avoid false positive p24 antigen determination. Cells were resuspended and identical aliquots ($1x10^6$/ml) of infected cells were futher cultured in 10 ml medium with drugs (AXD 455 or GC7 solved in Dimethylsulfoxide, DMSO) at the indicated concentrations [500 nM and 1000 nM], or in medium with DMSO as control for calculation of the

inhibition of virus replication [in %] (cf. Table 16). Inhibition of virus replications indicated in the diagrams (% inhibition as compared to DMSO-control cultures).

Example 48: Influenza

Viral infection: Madin-Darby canine kidney (MDCK) cells were cultivated in DMEM containing 10% fetal calf serum and antibiotics (100 U/ml penicillin, 0.1 mg/ml streptomycin). Benzo[g]quinoxaline compounds at different concentrations were added to the medium 1h prior infection. Medium was removed and cells were infected with 10 MOI of Aichi strain in PBS++ buffer (PBS, 0,2% BSA, 1 mM $MgCl_2$ and 0,9 mM $CaCl_2$) (PBS: phosphate buffered saline; BSA: bovine serum albumin) containing the compound at the respective concentration. After 1h infection, viruses were aspirated and cells were washed with PBS++ buffer. Subsequently, cells were incubated with DMEM supplemented with 0,2% BSA, 1 mM $MgCl_2$ and 0,9 mM $CaCl_2$ and 100 U/ml penicillin, 0.1 mg/ml streptomycin.

Hemagglutination assay: 100 µl of culture medium containing the viruses was transferred after 2, 4, 6, 8, 24 h postinfection to conical-bottom 96 well plates. Medium was diluted (1:2 to 1: 2,048) in ice–cold PBS (phosphate-buffered saline). Subsequently, an equal volume of chicken red blood cells was mixed with the dilutions and incubated on ice for 30 min. Loss of HA activity was monitored by formation of a visible pellet of blood cells.

Example 49: Cancer / Cytotoxicity

Tumor cell lines:

A549 cells (ATCC: No. CL-185)
Organism: *Homo sapiens* (human)
Designation: A549 [A-549]
Depositors: M. Lieber
Tissue: carcinoma; lung products: keratin morphology
Medium: Ham's F12K medium with 2 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 90%; fetal bovine serum, 10%

Jurkat cells (ATCC: No TIB 152)
Organism: *Homo sapiens* (human)

Designation: Jurkat, Clone E6-1
Depositors: A. Weiss Tissue: acute T cell leukemia; T lymphocyte Products: interleukin-2 (interleukin 2, IL-2) gamma interferon morphology: lymphoblast
Medium: RPMI 1640 medium with 2 mM L-glutamine adjusted to contain 1.5 g/l sodium bicarbonate, 4.5 g/l glucose, 10 mM HEPES (N-[2-hydroxyethyl]piperazine-N'-[2-ethansulfonic acid]), and 1.0 mM sodium pyruvate, 90%; fetal bovine serum, 10%

Proliferation assay:
To quantify cell proliferation, cellular metabolic activity was determined by oxidation of the tetrazolium salt WST-1 (Roche, Cat. No. 1 644 807) and subsequent photometric analysis. Tumor cells were cultivated either directly in 96 well microtiter plates (0,5 - $1x10^3$ cells per well in 100 µl appropriate medium as described above) or previously in tissue culture plates for longer compound exposure. Cells were incubated with different concentrations of compound for 3 days. Subsequently, 10 µl WST1 was added and mixtures were incubated for an additional 1h. The amount of converted formazan salt was quantified at least in four replicates by photometric analysis at 450 versus 655 nm.

Example 50: TNFalpha-Assay

Cells:
The effect of selected benzo[g]quinoxaline compounds on modulating inflammatory processes were evaluated by investigating the signal transduction pathways initiated by activation of the tumour necrosis factor (TNF) alpha receptor and leading to activation of NFkappa B. Cells used to examine activation of NFkappB pathways upon stimulation with tumour necrosis factor were two NIH 3T3 cell lines stably transfected with a construct consisting of a firefly luciferase reporter gene driven by a minimal promoter containing four NFkappa B binding sites (5'-GGG ACT TTC C-3'). For transfection experiments, NIH-3T3 cells were plated with 2 x 10^4 cells per well in 6 well-plates. After 24 hours cells had reached around 80% confluence and transfection with the NFkappaB promoter-luciferase construct using Lipofectamine Plus Reagent (Gibco/Life Technologies) was performed. Per well, 1.5 µg of vector DNA was applied according to the manufacturer's instruction. After 24 hours, the transfection medium was removed and 4 ml of DMEM / 10% FCS (fetal calf serum, Pansystems GmbH) (DMEM: Dulbecco's modified Eagle's medium)

containing 700 µg/ml G418 (Calbiochem) were added per well. Medium containing 700 µg/ml G418 was exchanged every two days. To avoid cells becoming completely confluent cells were transferred from the 6 well plate to a 10 cm dish after 5 days of selection. Around 10 days after start of selection all cells that have not been stably transfected died. To obtain single cell clones stably transfected with the NFkappaB promoter – luciferase construct limited dilution was performed. Therefore, 100 cells were plated per 96 well microtiter plate. After one week each well was analyzed microscopically for single clones. Single clones were propagated under selective pressure and examined for luciferase expression after TNF treatment.

Assay:

On day one, the 3T3 cell lines were plated in 96-well plates; $8x10^3$ cells per 100µl per well. The culture medium was DMEM containing 10% FCS, 1% glutamine, 250 µg/ml G418.

On day 2 (i.e. 24 hrs after plating), culture medium was changed to serum-free medium (DMEM, 1% glutamine, no G418, no phenol red, no FCS).

On day 3 benzo[g]quinoxaline compounds were added to each well; compounds were diluted in DMSO; final DMSO concentration in medium was less than 1%. After 30 min TNFalpha (10 ng/ml) (human, recombinant, SIGMA) was added and plates incubated at 37°C for 2 hrs. LucLite solution was prepared according to manufacturer's (Packard BioScience, Groningen Netherlands) instructions. The 96 well microtiter plate was adapted to room temperature and one volume of prepared LucLite Plus Reagent that was also equilibrated to room temperature was added to the wells. Upon incubation for 10 minutes in the dark the chemiluminescence signal was measured in the multiplate reader Victor V/2 (Wallac) (1 second count per well). The increase of luciferase activity in TNF-stimulated cells (with and without benzo[g]quinoxaline compounds) compared to untreated cells was calculated.

Example 51: HCV

Effect of compounds on levels of HCV replicons in the Huh-5-2 replicon cell line.

Benzo[g]quinoxaline compounds were tested for activity in the HCV replicon system described by Bartenschlager and coworkers (Lohmann et al, Replication

of subgenomic hepatitis C virus RNAs in a hepatoma cell line. Science 285, 110. 1999), which reproduces a crucial part of the HCV replication cycle, but does not lead to a productive infection or virus generation. The Huh-5-2 cell line carries the persistant bicistronic replicon I389luc-ubi-neo/NS3-3'/5.1 that expresses a firefly luciferase – ubiquitin – neomycin phosphotransferase fusion protein under the control of the HCV 5' UTR and the NS3-5B HCV polyprotein that harbors the cell culture adaptive mutation of NK5.1. (J. Virol. 75:4614-4624, 2001) and is driven by the EMCV-IRES. Autonomously replicating HCV RNA replicons are detectable by Northern blot or via expression of the luciferase part of the fusion protein in a luciferase reporter assay.

Huh-5-2 cells were grown in Dulbecco's modified minimal essential medium (Life Technologies GmbH, Karlsruhe, Germany) supplemented with 2 mM L-glutamine, nonessential amino acids, Penicillin (100 IU/ml) / Streptomycin (100 µg/ml) and 10% fetal calf serum in the presence of 0.5 mg/ml G418. Cells were routinely passaged three times a week at a dilution of 1:3 or 1:2. For Luciferase reporter assays, Huh-5-2 cells were seeded at 2500 cells per well in 96 well plates in medium without G418. After overnight incubation, benzo(g)quinoxaline compounds dissolved in DMSO were added to the medium at 20, 10, 5, 2.5 µM concentrations in duplicate samples. On day 3 after addition of compounds, Alamar Blue™ solution (Serotec), which contains a redox indicator, was added to the cells to measure cell proliferation and compound cytotoxicity. After incubation for 3-4 hours, fluorescence was monitored at 560 nm and 590 nm wavelengths with a Wallac 1420 multilabel counter. For the luciferase assay, the cells were subsequently washed twice with PBS without sodium hydrogen carbonate (Life Technologies GmbH, Karlsruhe), and luciferase activity was determined with the LucLite Plus Assay kit (Packard Bioscience B.V.) according to the manufacturer's instructions in a Wallac 1450 Microbeta Luminescence counter.

Example 52: General Kinase Assay

Basic protocol for performing a protein kinase assay (P81 filter binding):

Assays are performed in Eppendorf test tubes or in U-bottom polystyrene 96-well plates.

Assay components are sequentially mixed together as follows (tubes/plates kept at 20°C):

(kb: kinase reaction buffer as described in the individual protocols
e.g. Tris/$MgCl_2$/$MnCl_2$/Na_3VO_4/EGTA/DTT)

1) dispense 2 µl of a 20 % DMSO / kb solution of test compound
2) add 5 µl of an 8-fold concentrated solution of substrate peptide/protein in kb
3) add 5 µl of protein kinase solution (adequately diluted with kb) from an ice-chilled stock
4) immediately thereafter, add 28 µl ATP solution in kb (10/7 of final concentration containing 0.1-1 µCi of g-^{33}P-ATP)

Incubate 30-120 min at 20°C, then stop the kinase reaction by addition of excess EDTA (10 µl 100 mM).

Aliquots of the stopped kinase reaction are spotted on P81 phosphocellulose filter squares pre-soaked with 0.75 % H_3PO_4. The filters are subsequently washed three times in 0.75 % H_3PO_4 and once in methanol, then air-dried and placed into scintillation vials. After addition of Rotiscint cocktail, the vials are counted in a Packard Tricarb counter using an energy window 0-200.

Kinase Assay

Materials

kinase				-80°C
or	Oncogene			
poly Glu-Tyr	Sigma	(# P275)	3 µg/µl	-20°C
ATP	Sigma		100 mM	-20°C
γ-^{33}P-dATP	Amersham		10 µCi/µl	4°C
Vanadate (Na_3VO_4)	Merck		100 mM	-20°C
staurosporine	Calbiochem		10 mM	4°C
DMSO	Merck			RT
P81	Upstate biotechnology			RT
0.75% phosphoric acid	inhouse			RT
EDTA	inhouse		0.5 M pH 7.4	RT

Assay conditions

ca 2 U kinase per reaction

30 ng/µl poly Glu, Tyr
20 µM ATP
0.2 µCi γ-^{33}P-dATP per reaction
60 min RT
Reference inhibitor: staurosporine
0.3 - 0.1 - 0.033 - 0.011 µM 03/02: to reduce to 0.1 µM and less

Solutions (prepare freshly for each experiment)

kinase buffer (kb), 5 ml		stock soln.	
50 mM TRIS/HCl pH 7.5	250 µl	1 M	RT
10 mM $MgCl_2$	50 µl	1 M	RT
10 µM Na_3VO_4	0.5 µl	100 mM	4°C
1 mM DTT	5 µl	1 M	-20°C
	4694.5 µl	H_2O	

kb / 20 % DMSO, 200 µl
40 µl DMSO + 160 µl kb

enzyme mix (prepare as late as possible, keep on ice)
for 1 assay: ca 2 units, e.g.1 µl 2.1 U/µl kinase + 4 µl kb
for **X** assays: **X** • 2 µl 2.1 U/µl kinase + **X** • 3 µl kb on ice

substrate mix
for 1 assay: 0.4 µl 3 µg/µl poly Glu, Tyr + 4.6 µl kb → 240 ng/µl
for **X** assays: **X** • 0.4 µl 3 µg/µl poly Glu, Tyr + **X** • 4.6 µl kb on ice

ATP mix
1st dilution: 4 µl 100 mM ATP + 196 µl kb → 2 mM ATP
2nd dilution: 196 µl 2 mM ATP + 1204 µl kb → 280 µM ATP
3rd dilution: 150 µl 280 µM ATP + 1350 µl kb → 28 µM ATP
for 1 assay: In C-lab: 28 µl 28 µM ATP + 0.1 µl 10 µCi/µl γ-^{33}P-dATP
for **X** assays: In C-lab: X • 28 µl 28 µM ATP + X • 0.1 µl 10 µCi/µl γ-^{33}P-dATP
(addition of radioactivity to be performed in C laboratory)

Staurosporine (STP) serial dilution
1st dilution: 1 µl 10 mM STP + 99 µl DMSO → 100 µM STP in DMSO
STP (6 µM) 3 µl 100 µM STP + 7 µl DMSO + 40 µl kb (→ 6 µM STP in 20 % DMSO)
STP (2 µM) 15 µl 6 µM STP + 30 µl kb / 20 % DMSO

STP (0.67 µM) 15 µl 2 µM STP + 30 µl kb / 20 % DMSO

STP (0.22 µM) 15 µl 0.67 µM STP + 30 µl kb / 20 % DMSO

Compound dilution (BQ 96 well plate, 5 mM)

1st dilution: 1 µl 5 mM compound + 4 µl DMSO → 5 µl 1000 µM compound in DMSO

2nd dilution: 5 µl 1000 µM comp + 20 µl kb → 25 µl 200 µM comp in kb / 20 % DMSO

stop buffer (1 ml)

100 mM EDTA	200 µl	0.5 M	RT
	800 µl	H_2O	

Assay total 40 µl, duplicates in brackets: sample names

2 µl compound / STP mix (20 x conc in 20 % DMSO)

5 µl substrate mix (8 x conc = 240 ng/µl)

5 µl enzyme mix

28 µl ATP mix (1.4 x conc = 28 µM)

Positive control: 2 µl kb / 20 % DMSO instead of compound / AX7081 (C+)

Negative control: 2 µl kb / 20 % DMSO + 10 µl EDTA (EDTA)

→ each reaction in duplicate

- pipet 2 µl of compound mix or STP mix or kb / 20 % DMSO to the appropriate vial
- combine enzyme mix with substrate mix (1 vol enzyme + 1 vol substrate) on ice
- add 10 µl of combined enzyme / substrate mix to each vial
- perform next steps in C-laboratory without delay
- add appropriate amount of γ-^{33}P-dATP to ATP mix (0.1 µl γ-^{33}P-dATP / 28 µl 28 µM ATP)
- add 28 µl of ATP complete mix to each vial
- incubate for 60 min at room temperature
- add 10 µl of 100 mM EDTA to each vial (except "EDTA first" control)
- pre-wet appropriate number of P81 filter squares with 0.75 % phosphoric acid
- dry (Kimwipes or paper towel), place on aluminum foil or parafilm
- spot 10 µl of each assay onto the center of a P81 filter
- spot 5.6 µl of ATP complete mix onto the center of a P81 filter (ATP)
- use two filters without spotted radioactivity as control for wash bath
- wash the filters three times with 0.75 % phosphoric acid for 10 min each on shaker
- wash the filters once with methanol
- dry filters for 10 min
- transfer the filters to labeled scintillation vials

- pipet 5.6 µl of ATP mix into a scintillation vial (input) [duplicate]
- add 3 ml scintillation cocktail to each vial
- read in scintillation counter

Example 53: Validation of HBV targets SRPK1 and SRPK2

1. Plasmid construction

Plasmid pGEX-HBV-C3 contains the entire coding sequence of HBV core protein (amino acid 1 to 183; subtype ayw) cloned in frame with the glutathione-S-transferase gene into the pGEX-5X (Pharmacia) vector. Plasmids pGEX-HBV-C1 and pGEX-HBV-C2 encode GST-fusions with N-terminally truncated core proteins that start at amino acid position 119 or 30, respectively. The insert from pGEX-HBV-C3 encoding for full length HBV core protein was cloned into the eucaryotic expression vector pcDNA3. In this construct serines 155, 162 and 170 of HBV core protein were mutated to alanine and an N-terminally truncated mutant starting at amino acid position 119 was inserted into pGEX-5X for generation of GST-HVB-C1-AAA fusion protein. The full length SRPK1 coding sequence was PCR-amplified from HeLa cell cDNA and fused to an N-terminal FLAG epitope by insertion into pRK-FLAG vector. Plasmid pcDNA-SRPK2-VSV expresses a functionally active VSV-tagged version of SRPK2 from a pcDNA3 vector background.

2. In-vitro kinase assay

Confluent 10 cm dishes of Huh-7 cells were lysed in 500 µl lysis buffer per dish containing 50 mM HEPES pH 7.5, 150 mM NaCl, 0.5% Triton X-100, 10% glycerol, 1 mM EDTA (ethylene diamine tetraacetate), 2 mM $MgCl_2$ plus additives (10 mM sodium pyrophosphate, 10 mM sodium fluoride, 1 mM orthovanadate, 10 µg/ml aprotinin, 10 µg/ml leupeptin, 1 mM PMSF (phenylmethylsulfonyl fluoride), 0.2 mM DTT (dithiothreitol). Lysates were cleared by centrifugation (10 min, 13000 rpm, 4°C) and 300 µl per sample were then subjected to in-vitro association with either GST or GST-HBV-C1, -C2 or –C3 fusion proteins pre-bound to glutathione-sepharose beads for 2.5 hours at 4°C. The beads were then washed twice with 500 µl lysis buffer without additives and twice with 300 µl kinase buffer (50 mM HEPES (N-[2-Hydroxyethyl]piperazine-N´-[2-ethansulfonic acid]) pH 7.5, 100 mM NaCl, 10 mM $MgCl_2$). Kinase reactions were performed in 25 µl kinase buffer supplemented with 50 µM ATP and 1 µCi [γ-^{32}P]ATP for 5

min at 37°C. Reactions were stopped by addition of 20 µl 3x SDS sample buffer (100 mM Tris pH 6.8, 3% SDS, 30% glycerol, 5% β-mercaptoethanol). Samples were subjected to gel electrophoresis on 12.5% gels and the Coomassie–stained gels were then autoradiographed.

3. In-gel kinase assay

In-vitro associations were performed essentially as described above. Beads were washed three times with lysis buffer without additives and bound proteins were eluted by incubation for 10 min at 50°C in 2 x SDS sample buffer. SDS-PAGE was performed on 10% minigels containing either 75 µg/ml GST or GST-HBV-C1 protein co-polymerised in the separating gel. Gels were incubated twice for 30 min in 100 ml 20% isopropanol / 50 mM Tris-HCl (Tris-(hydroxymethyl)-aminomethane-hydrochloride) pH 8.0 and then washed for 1 hour in 250 ml 50 mM Tris-HCl pH 8.0 / 5 mM β-mercaptoethanol. To denature proteins, gels were incubated twice for 30 min in 100 ml 6M guanidine-hydrochloride and then renatured for 16 hours in 250 ml 50 mM Tris-HCl pH8.0 / 5 mM β-mercaptoethanol / 0.04% Tween 40 (polyoxyethylenesorbitan monopalmitate) at 4°C (five changes). Gels were then equilibrated for 1 hour in 20 ml 40 mM HEPES-NaOH pH 7.5 / 100 mM NaCl / 2 mM DTT / 10 mM $MgCl_2$. The kinase reaction was carried out for 1 hour in 15 ml 40 mM HEPES-NaOH pH 7.5 / 100 mM NaCl / 10 mM $MgCl_2$ / 0.5 mM EGTA (ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid) / 75 µCi [γ-^{32}P]ATP / 10 µM ATP gels were then washed extensively in 5% TCA (trichloracetic acid) / 1% sodium pyrophosphate until washes were free of radioactivity (usually five changes). Gels were then Coomassie-stained and dried and autoradiography was performed.

4. 16-BAC/SDS-PAGE

16-BAC gels were cast as 0.75 mm thick minigels. The 7.5 % separating gel was prepared by mixing 1.8 g urea, 2.5 ml of a acrylamide / N,N′-methylenbisacrylamide solution (30% / 0.8% w/v), 0.3 ml 2% N,N′-methylenbisacrylamide (w/v), 5 ml 2 x separating gel buffer (KH_2PO_4, 2.05%, w/v; H_3PO_4, 1% v/v), 0.5 ml 1.45% ascorbic acid (w/v, freshly prepared) and 16 µl 0.14% $FeSO_4 \cdot 7H_2O$ (w/v, freshly prepared). The volume was adjusted with water to 9.6 ml and after degassing the solution for 10 min, the polymerization was initiated by adding 0.4 ml H_2O_2 (1:1200 dilution of 30% H_2O_2) and the top

surface was overlaid with 1 x separating gel buffer. The 4% stacking gel consisted of 1 g urea, 1.3 ml of a acrylamide / N,N'-methylenbisacrylamide solution (30% / 0.8% w/v), 1.16 ml 2% N,N'-methylenbisacrylamide (w/v), 2.5 ml 4x stagging gel buffer (0.5 M KH_2PO_4, pH 4.1), 0.5 ml 1.45% ascorbic acid (w/v) and 8.5 µl 0.14% $FeSO_4 \cdot 7H_2O$ (w/v). The volume was adjusted with water to 9.5 ml and after degassing the solution for 10 min, the polymerization was initiated by adding 0.5 ml H_2O_2 (1:750 dilution of 30% H_2O_2). After 1 hour of polymerization, gels were kept at 4°C and used the next day.

Aspirated beads from in-vitro association experiments were mixed with 30 µl freshly prepared sample buffer (0.6 g urea, 1.25ml 10% 16-BAC (benzyldimethyl-n-hexadecylammonium chloride), 200 µl 87% glycerol, 90 µl 1M DTT, 12.5 µl 2 mg/ml aprotinin) and incubated for 10 min at 37°C prior to sample loading. The electrode buffer used was 1.126% (w/v) glycine, 0.35% (v/v) H_3PO_4 and 0.1% 16-BAC was included in the upper electrode buffer. Electrophoresis was carried out towards the cathode with an initial current of 10 mA per gel, which was later increased to 20 mA per gel. Electrophoresis was terminated 10 min after the Schlieren line had run out of the bottom of the gel.

The gel was fixed for 1 hour in 10% (v/v) acetic acid / 40% (v/v) methanol and then Coomassie-stained and destained. For equilibration, gels were incubated for 10 min in 100 mM Tris-HCl pH 6.8, 10 min in a solution consisting of 50 mM Tris-HCl pH 6.8, 30% (v/v) glycerol, 6M urea and 2% SDS and then for a further 10 min in the same solution containing 10 mg/ml DTT. The gel was then cut in strips using a glass plate and the strips were then positioned on top of the flat stacking gel surface of the 10% second dimension SDS gels. Electrophoresis was carried out towards the anode with an initial current of 5 mA per gel, which was later increased to 20 mA per gel. Electrophoresis was terminated when the Coomassie blue had eluted from the bottom of the gel and gels were then Coomassie-stained and then destained. For subsequent analysis by mass spectrometry, gels were washed 3 times for 10 min with water and the spots of interest were excised from the gel. For analytical purposes, in-vitro associations were performed essentially as described. Protein elution was achieved by directly adding 16-BAC sample buffer to the aspirated beads. For preparative purposes, eight confluent 10 cm dishes of Huh-7 cells were lysed in 550 µl lysis buffer and 6 in-vitro associations of 670 µl lysate with GST-HBV-C1 were performed in parallel. Eluted proteins were subjected to 16-BAC/SDS-PAGE

and the six spots of the protein of interest were pooled and then subjected to analysis by mass spectrometry.

5. Mass spectrometry

In-gel digestion: The excised gel plugs were washed 2 times in 100 mM $(NH_4)_2CO_3$ (ammonium carbonate), pH 7.8, 2 times in 100 mM $(NH_4)_2CO_3$ / acetonitrile (60/40) and dried by vacuum centrifugation. For reduction the plugs were re-swollen in 100 mM $(NH_4)_2CO_3$ containing 10 mM DTT, and were incubated for 45 min at 56°C. Thereafter the tubes were chilled to room temperature and the liquid was replaced with roughly the same volume of 55 mM iodoacetamide, 100 mM $(NH_4)_2CO_3$. Samples were incubated for 30 min in the dark. Iodoacetamide solution was removed and the gel plugs were washed and dried as described above. Trypsin (15 ng/µl) was added to the dry gel pieces and incubated on ice for 1h for re-swelling. After this time sufficient digestion buffer was added to cover the gel pieces and the digestion was continued at 37°C over night. The supernatant was transferred to a sample cup and dried in a speed vac vacuum concentrator. The gel pieces were washed 2 x with 25 mM $(NH_4)_2CO_3$, and 2x with 25 mM $(NH_4)_2CO_3$/ acetonitrile (40/60) and two times with acetonitrile (50%) containing 5% formic acid. All supernatants were collected and successive dried in a speed vac.

Desalting and concentration: Samples were desalted and concentrated using ZipTips. The dried peptides were resolubilized in 20 µl 5% formic acid, loaded onto the tip, and washed with 5% formic acid / 5% methanol. The peptides were eluted with 60% methanol / 0.5% formic acid.

MALDI-MS: A Bruker Reflex MALDI time-of -flight mass spectrometer (Bruker-Daltonics, Bremen, Germany) was employed for peptide mass mapping in positive ion reflector mod. Acceleration voltage was 20 kV. For co-precipitation of analyte and matrix according to the dried droplet method the analyte solution and the matrix solution (20 mg/ml α-cyano-4-hydroxycinnamic acid in 70% acetonitrile) were mixed in equal portions (0.5 µl) on the MALDI target and dried. The dry crystalline deposit was washed with a small volume of ice cold 0.1% TFA (trifluoroacetic acid).

ESI-MS: MS/MS of peptides generated by in-gel digestion was performed by nano-ESI on a Q-TOF mass spectrometer (Micro Mass, Manchester, UK). The

cone voltage was 50 V. The quadrupole analyser was used to select precursor ions for fragmentation in the hexapole collision cell. The collision gas was argon at a pressure of 6-7x10^{-5} Torr. The collision energy was 20 - 30V. The data were processed using a Mass Lynx Windows NT PC system.

6. Cell culture, transfections, cell lysate processing

Huh-7 and Cos-7 cells were cultured in Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum (FBS). For transfection experiments, COS-7 cells were seeded at 3.5 x 10^5 per well into 6-well dishes 20 h before transfection. Cells were incubated for 4h in 1.0 ml serum-free medium containing 9 µl Lipofectamine (Gibco-BRL) and 1.5 µg Plasmid DNA per well. The transfection mixture was then supplemented with 1 ml of medium containing 20% FBS and 20 h later, cells were either lysed or incubated in phosphate-free medium in the presence with 100 µCi/ml [^{33}P] orthophosphate for 3 hours prior to cell lysis. Cells were lysed in 150 µl buffer containing 50 mM Hepes pH 7.5, 150 mM NaCl, 0.5 % Triton X-100® (t-octylphenoxypolyethoxyethanol), 10% glycerol , 1 mM EDTA, 2 mM $MgCl_2$ plus additives (10 mM sodium pyrophosphate, 10 mM sodium fluoride, 1 mM orthovanadate, 10 µg/ml aprotinin, 10 µg/ml leupeptin, 1 mM PMSF, 0.2 mM DTT). Lysates were cleared by centrifugation (10 min, 13000 rpm, 4°C) and 120 µl per sample were then subjected to in-vitro association with either GST or GST-HBV-C1 or to immuno-precipitation with monoclonal anti-FLAG (Sigma) or anti-VSV (Boehringer) antibodies or polyclonal anti-HBV core protein antibody (DAKO). For subsequent immunoblotting, the same antibodies or monoclonal anti-SRPK1 or anti-SRPK2 antibodies (Transduction Laboratories) were used.

For measurement of specific kinase activity immuno-precipitates were washed twice with 300 µl lysis buffer without additives and twice with 200 µl kinase buffer (50 mM Hepes pH 7.5, 100 mM NaCl, 10 mM $MgCl_2$). Kinase reactions were performed in 25 µl kinase buffer supplemented with 50 µM ATP, 1 µCi [γ-^{32}P]ATP and similar amounts of either GST-HBV-C1 or GST-HBV-C1-AAA for 5 min at 37°C. Reactions were stopped by addition of 20 µl 3 x SDS sample buffer. Samples were subjected to gel electrophoresis on 12.5% gels and the Coomassie–stained gels were then autoradiographed.

7. Total cellular kinase assay

Transfected cells were lysed in sixwells in 150 µl of the buffer described above without sodium pyrophosphate. Lysates were pre-cleared by centrifugation and 120 µl were transferred into tubes containing washed and aspirated GST-HBV-C1 bound to glutathione beads. Kinase reactions were started by adding $MgCl_2$ to a final concentration of 10 mM, ATP to a final concentration of 50 µM, and 1 µCi [γ-^{32}P]ATP per sample. Samples were incubated for 5 min at 25°C under shaking. And reactions were stopped by adding 7 µl EDTA. Beads were then spun down, the supernatants removed and GST-HBV-C1 eluted by boiling in SDS sample buffer.

8. SRPK2 kinase assays for compound screening

HEK-293 cells were transfected with pcDNA-SRPK2-VSV in sixwell plates by the calcium-phosphate precipitation method. 24h post transfection, cells were washed and lysed with 500 µl of lysis buffer (20 mM Hepes pH 7.5, 150 mM NaCl, 1 mM EDTA, 10 µg/ml leupeptin, 1 mM PMSF, 1% Triton-X-100) per well. Lysates were cleared by centrifugation, 1/10 of the lysate was used to confirm SRPK2 expression by Western blotting, 9/10 were used for immuno-precipitation with an anti-VSV antibody. Immuno-precipitates were washed and incubated with test compounds for 5 min on ice. Kinase reactions were performed in the presence of 10 µM ATP and 2.5 µCi ^{33}P-ATP in 40 mM Hepes pH 7.5, 10 mM $MgCl_2$, 2 mM DTT for 30 min at 30°C using 5 µg myelin basic protein as a substrate. The reaction products were separated by SDS-PAGE.

Results:

To analyse whether cellular protein kinases can associate with and phosphorylate the HBV core protein, we used total cell lysates from Huh-7 cells for in-vitro association experiments with various GST-HBV core fusion proteins as baits. As can be seen in Fig. 1, all three GST-HBV core fusion proteins tested were found to be phosphorylated in an in-vitro kinase assay. The C-terminal part of HBV core protein was sufficient for kinase binding and served well as a kinase substrate (Fig. 1). To examine whether the cellular kinase(s) catalysing HBV core protein phosphorylation associate specifically, we subjected samples of GST- and GST-HBV core-associated proteins to SDS gels containing either co-polymerised GST or GST-HBV-C1 and performed an in-gel kinase assay. Two kinases of apparent molecular weights of 90 kDa and 110 kDa were found to specifically associate with the GST-HBV core fusion proteins

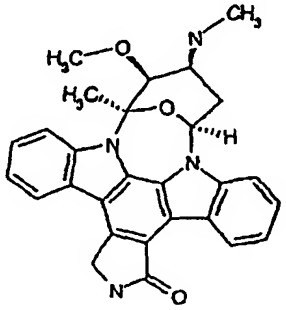
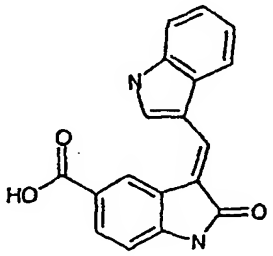
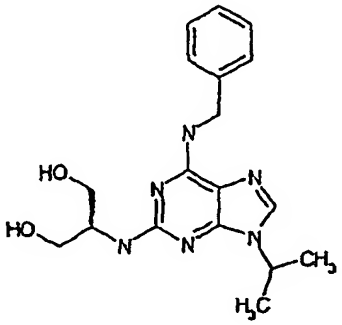
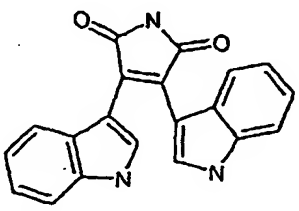
C1, C2 and C3. These two kinases specifically phosphorylated GST-HBV-C1, but not the GST in the control gel, and also represented two major GST-HBV-C1-phosphorylating kinases detected in total cell lysates. A 45 kDa kinase phosphorylating GST-HBV-C1 was also detected in total cell lysates, but not found to associate significantly with the GST-HBV core fusion proteins in these experiments (Fig. 2). To purify these kinases, we separated GST- and GST-HBV-C1-associated proteins from Huh-7 cells by the two-dimensional 16-BAC/SDS-PAGE method and employed again an in-gel kinase assay with GST-HBV-C1 as substrate to identify the protein spots representing the specifically associated kinases (Fig. 3). The same spots were more intensely stained with Coomassie in parallel gels containing no co-polymerised substrate protein and were excised from those for subsequent analysis by mass spectrometry (data not shown). Tryptic fingerprint analysis by MALDI-TOF-MS identified human SRPK1 as candidate protein. This was confirmed by MS/MS analysis of selected peptides generated by in-gel digestion, which allowed sequencing of the two peptides LEESSTIGQDQTLMER and EINCNGVLEVLNYTQNSNNETLR representing amino acids 330 to 345 and 353 to 375 in the human serine kinase SRPK1. This result could be confirmed by immunoblot analysis using anti-SRPK1 antibody and the 115 kDa kinase could be identified as the related kinase SRPK2. Transfection of either FLAG-SRPK1 or SRPK2-VSV expression plasmids into cells lead to increased levels of specifically GST-HBV-C1-associating SRPK1 or SRPK2 and the transiently expressed kinases could be detected in anti-FLAG or anti-VSV immunoblots, respectively (Fig. 4).

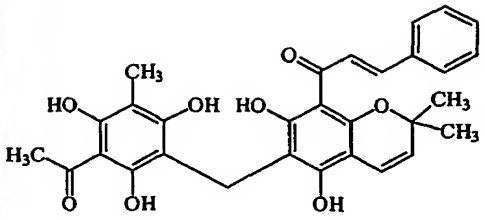
In-vivo, the HBV core protein is mainly phosphorylated on three serine residues in its C-terminal part (serines 155, 162 and 170). Mutation of all three serines to alanines strongly reduced HBV core protein phosphorylation in cells (Fig. 5). Importantly, both SRPK1 and SRPK2 showed the same substrate specificity in-vitro as the cellular kinases in-vivo and only weakly phosphorylated GST-HBV core protein lacking the three in-vivo phosphorylation sites (Fig. 6). Moreover, overexpression of either SRPK1 or SRPK2 correlated with increased GST-HBV-C1 phosphorylation by total cellular proteins in-vitro (Fig. 7). Taken together these results define SRPK1 and SRPK2 as candidate kinases likely to catalyze HBV core protein phosphorylation in-vivo and thereby playing an essential role for HBV replication.

To perform initial tests for compounds that inhibit SRPK2 activity in a cellular assay, SRPK2 was overexpressed in HEK-293 cells, immunoprecipitated and

incubated with different concentrations of test compounds before in-vitro kinase assays were performed. The five compounds listed in the following Table 18 showed inhibition of SRPK2 kinase activity with an IC50 between 5 and 20 µM.

Table 18: Inhibition of SRPK2 by selected compounds A to E:

compound	name	structure	IC50 SRPK2 (µM)
A	staurosporine		5-10
B	3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic		10
C	roscovitine		20
D	2,3-bis-(1*H*-indol-3-yl)-maleimide		20

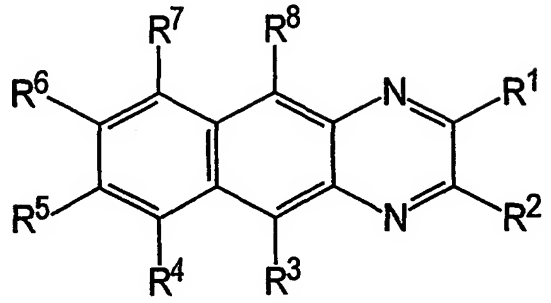
E	rottlerin		**20**

From the results observed with staurosporine, 3-(1*H*-indol-3-yl-methylene)-2-oxo-2,3-dihydro-1*H*-indole-5-carboxylic, roscovitine, 2,3-bis-(1*H*-indol-3-yl)-maleimide and rottlerin, these compounds were revealed as inhibitors of SRPK2 and as candidates for anti-HBV compounds.

From the foregoing discussions and examples, additional embodiments of the present invention will be apparent to those skilled in this art. All such obvious additional embodiments are included in the scope of the invention as contemplated and described herein and in the claims that follow. The publications cited above are incorporated herein by reference.

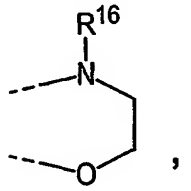
Claims

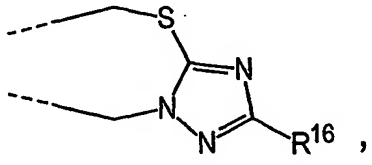
1. Compounds having the general formula (I):

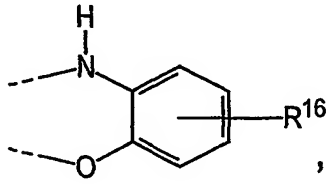


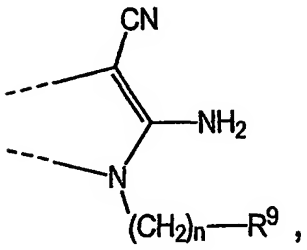
wherein:

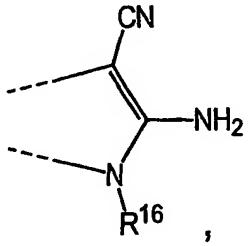
R^1 and R^2 are independently of each other $-(CH_2)_p-NH-(CH_2)_n-R^9$, $-(CH_2)_s-S-(CH_2)_m-R^{10}$, $-(CH_2)_m-O-(CH_2)_p-R^{11}$, $-(CH_2)_r-R^3$, $-CH=CH-R^{11}$, $-(CH_2)_m-CH(OH)-(CH_2)_p-R^{11}$, $-(CH_2)_q-R^{11}$, $-R^9$, $-R^{10}$, $-R^{12}$, $-R^{13}$,

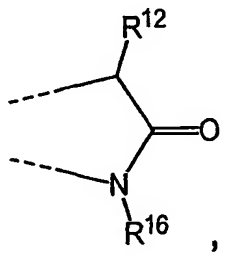
 ,

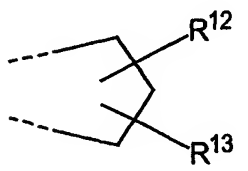
 ,

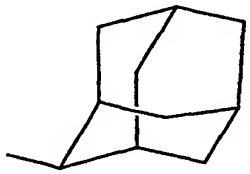
 ,

 ,

 ,

 ,

 ,

 ;

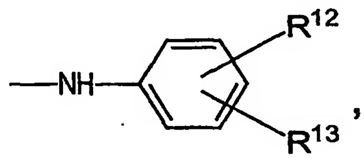
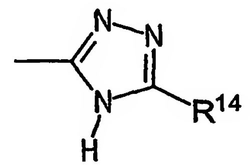
R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other $-H$, $-F$, $-Cl$, $-Br$, $-I$, $-SO_3H$, $-SO_3NH_2$, $-(CH_2)_s-COOR^{16}$, $-(CH_2)_p-COOR^{17}$, $-OR^{16}$, $-SR^{16}$, $-NR^{16}R^{17}$, $-OOCR^{16}$,

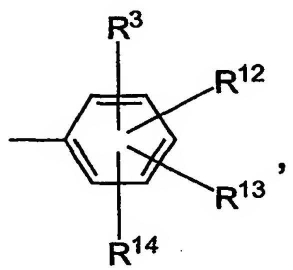
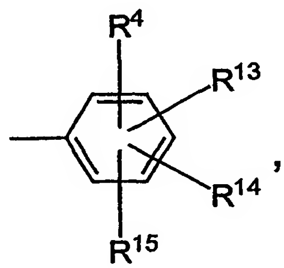
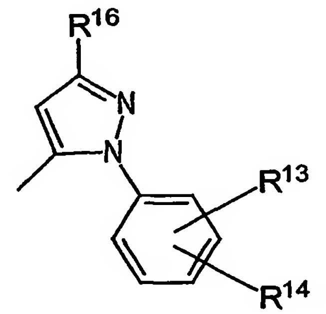
—OOCR^{17}, —NH–CO–R^{16}, —NH–CO–R^{17}, —CO–NH–R^{16}, —CO–NH–R^{17}, —NO_2, —N_3, —CN, —OCN, —NCO, —SCN, —NCS, —CO–R^{16}, —CO–R^{17}, —COCN, —CONR^{16}R^{17}, —SOR^{16}, —SOR^{17}, —SO_2R^{16}, —SO_2R^{17}, —SO_3R^{16}, —SO_3R^{17}, —OCF_3;

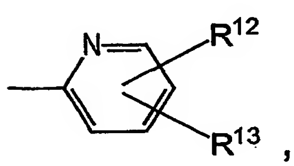
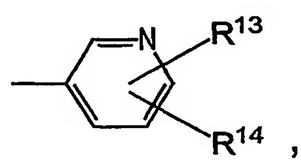
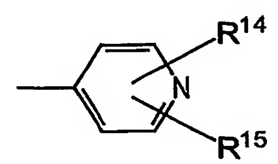
R^9, R^{10}, and R^{11} are independently of each other —CN, —NR^{16}R^{17},

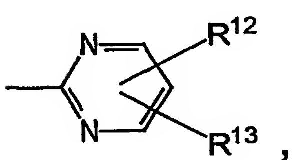
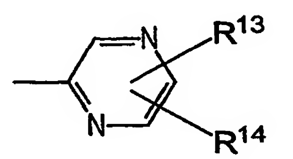
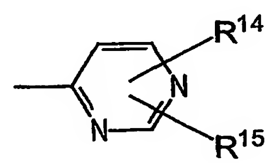
—NHR^{16},

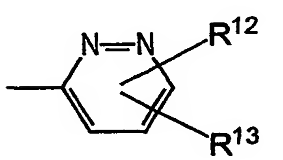
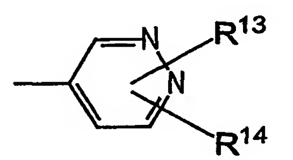
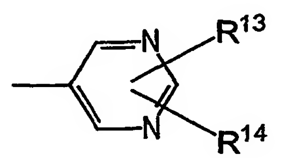
—NHR^{17},

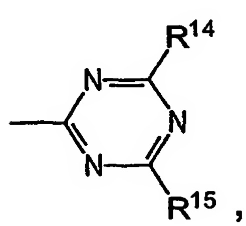
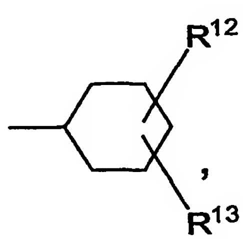
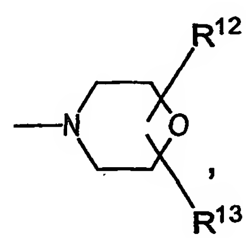



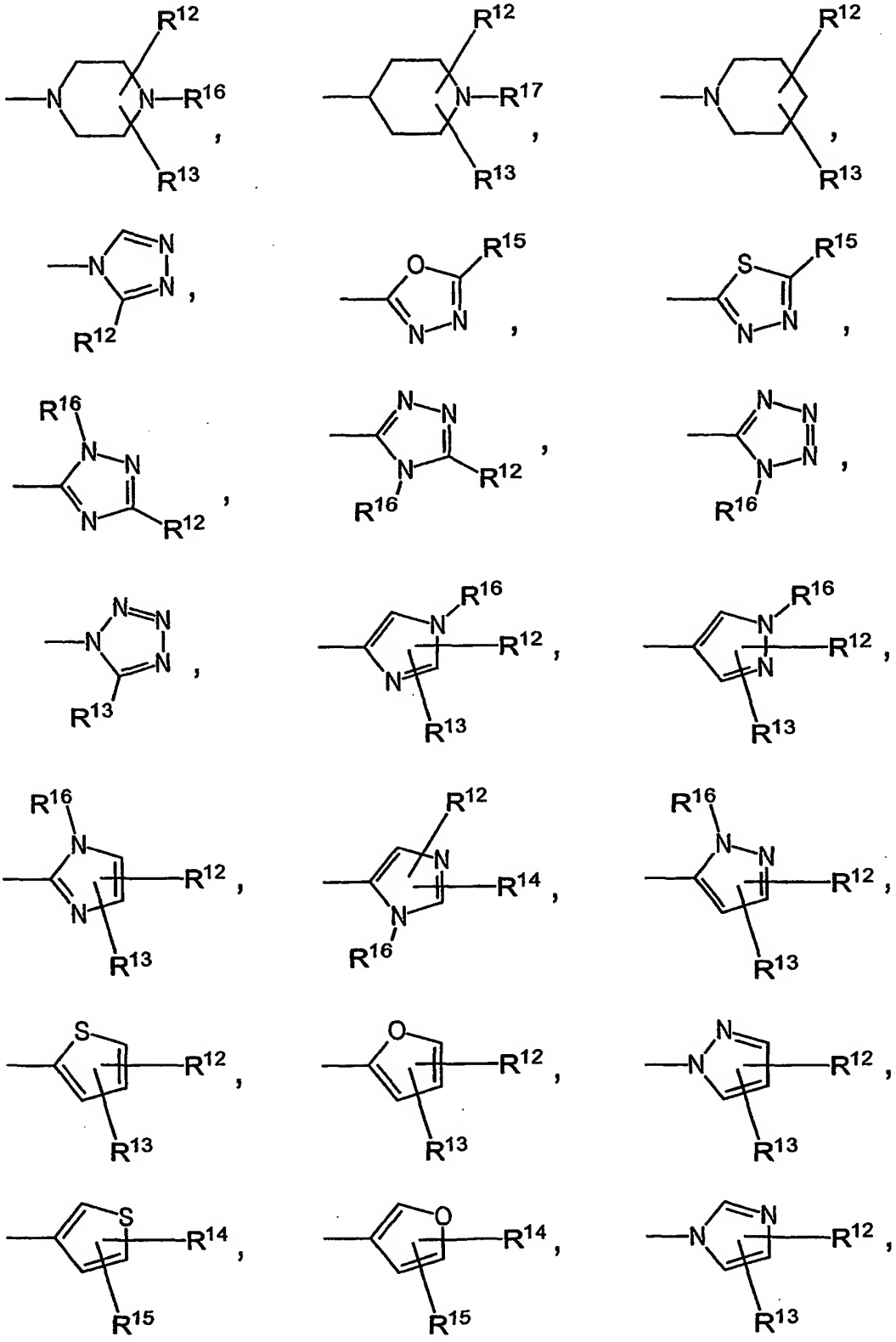




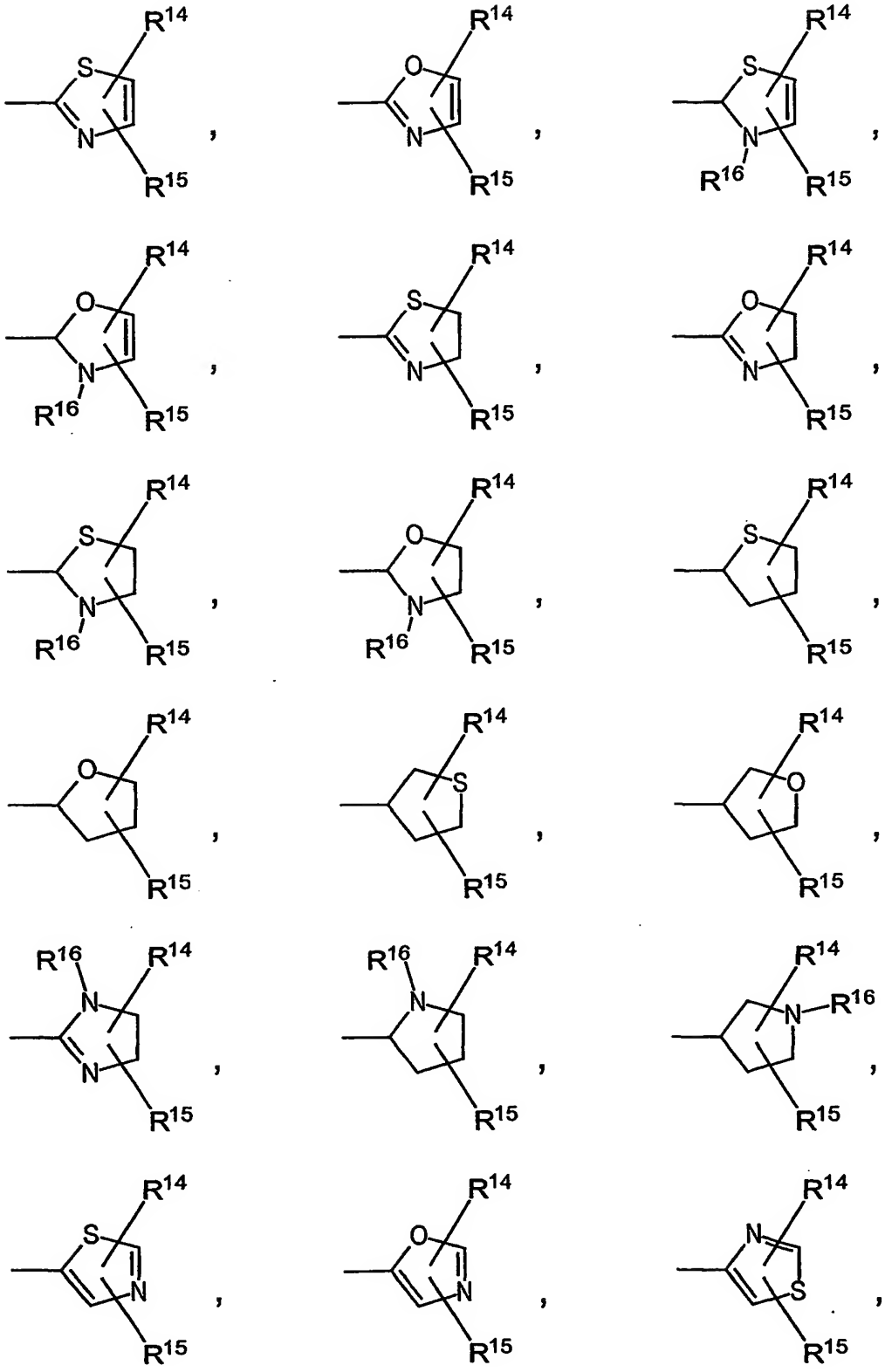




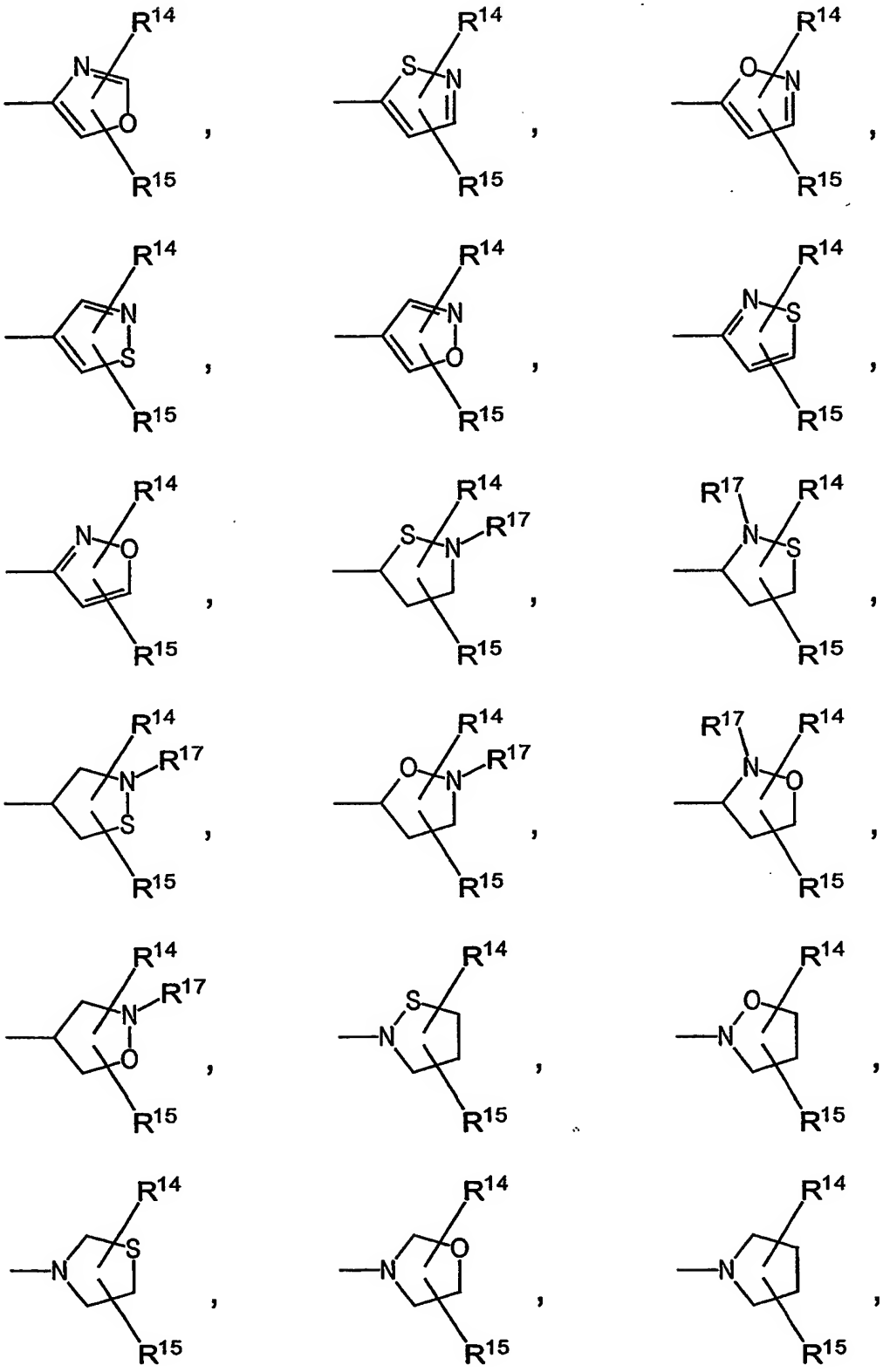




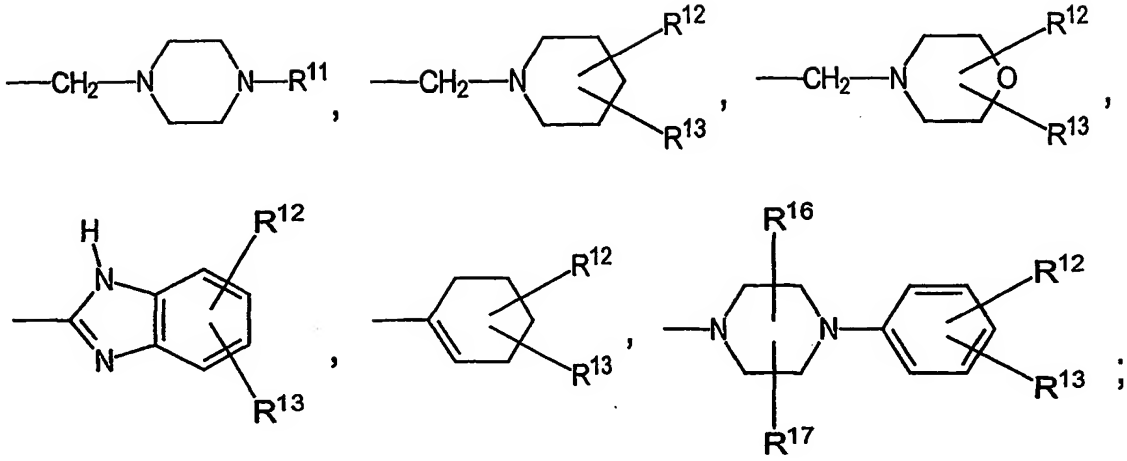








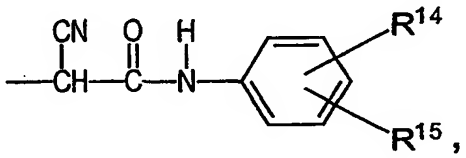




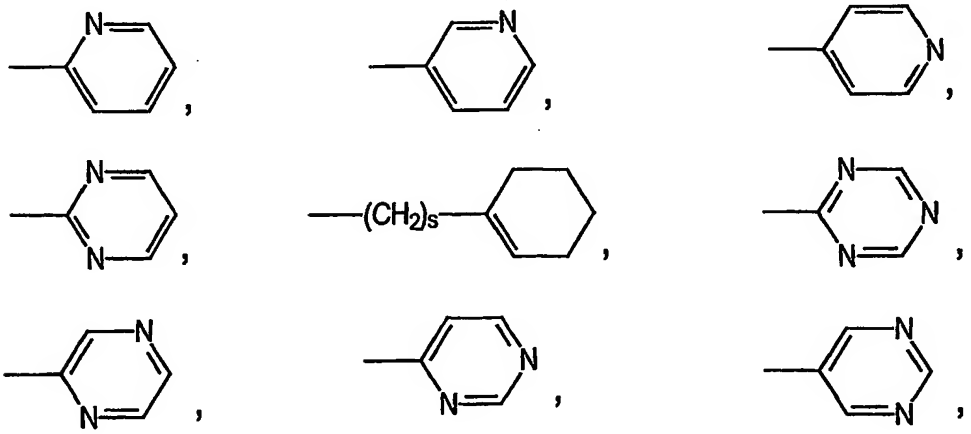
R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17},

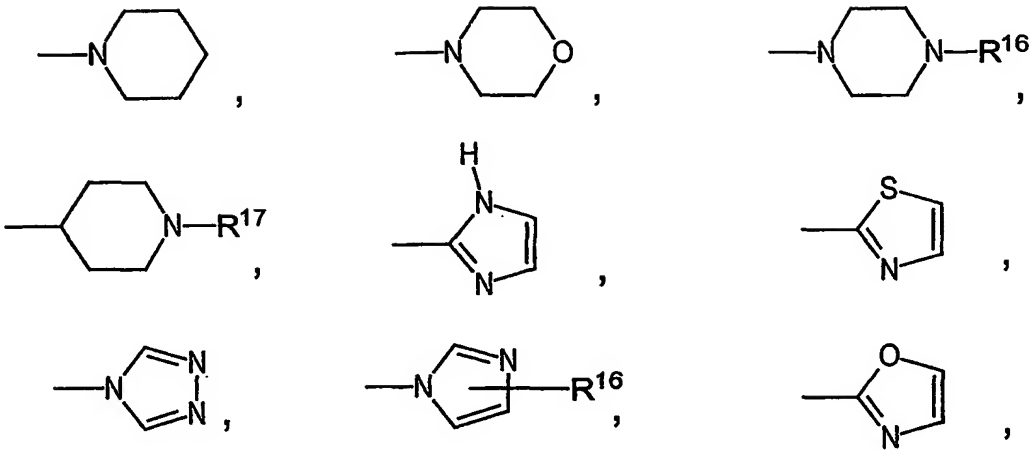
—$CH(COOR^{16})(COOR^{17})$,

—$CH(CN)(COOR^{16})$,



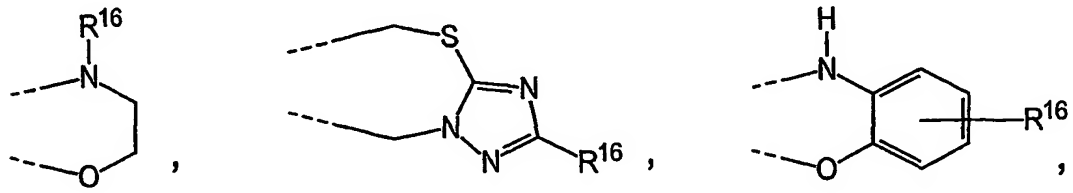
R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —cyclo–C_4H_7, —cyclo–C_3H_5, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —$CH=CH_2$, —CH_2–$CH=CH_2$, —Ph, —CH_2Ph, —C_2H_4Ph, —$CH(CN)_2$, —CF_3, —CCl_3, —CBr_3, —C_2F_5, —$(CH_2)_r$–OH, —CH_2F, —CH_2Cl, —CH_2Br, —CH_2I, —CHF_2, —$CHCl_2$, —$CHBr_2$, —$(CH_2)_r$–SH, —C_6H_4–CH_3, —$C_6H_3(CH_3)_2$,

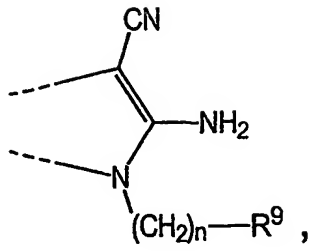
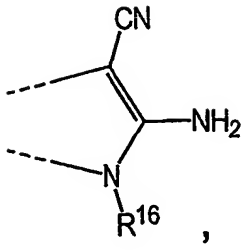
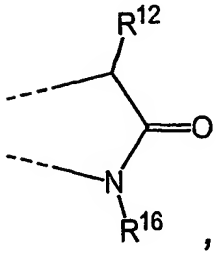
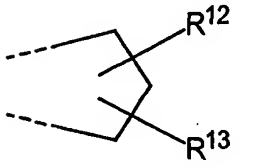
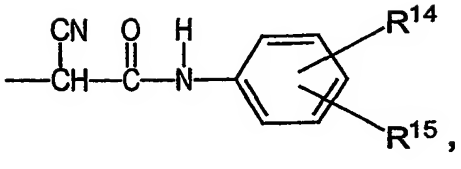
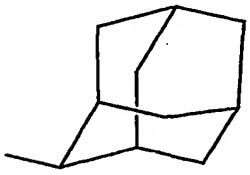




m is an integer from 0 – 6,
n is an integer from 0 – 6,
p is an integer from 0 – 6,
q is an integer from 0 – 6,
r is an integer from 1 – 6,
s is an integer from 0 – 6,
and/or the corresponding N-oxides in position 1 and/or 4 of these compounds;
and/or the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and/or pharmaceutically acceptable salts of these compounds.

2. Compound according to claim 1 wherein:
R^1 and R^2 are independently of each other $-(CH_2)_p-NH-(CH_2)_n-R^9$, $-(CH_2)_s-S-(CH_2)_m-R^{10}$, $-(CH_2)_m-O-(CH_2)_p-R^{11}$, $-(CH_2)_r-R^3$, $-CH=CH-R^{11}$, $-(CH_2)_m-CH(OH)-(CH_2)_p-R^{11}$, $-(CH_2)_q-R^{11}$, $-R^9$, $-R^{10}$, $-CH(COOR^{16})(COOR^{17})$, $-CH(CN)(COOR^{16})$,



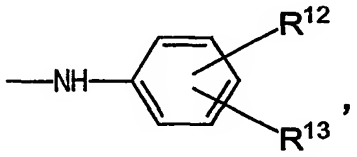
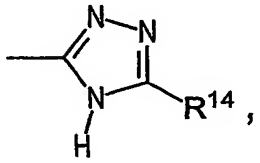
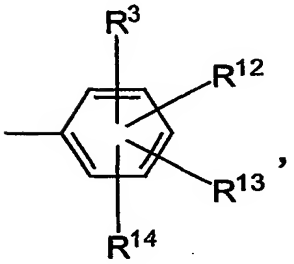
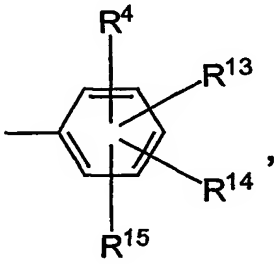
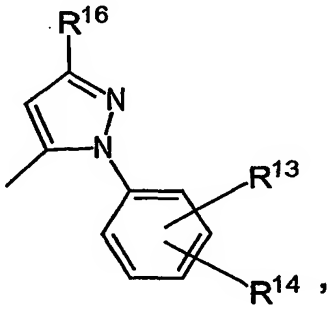
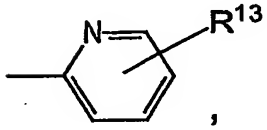
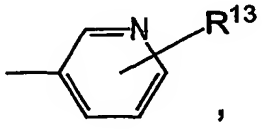
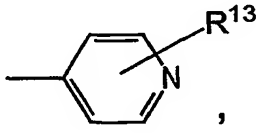
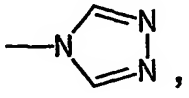
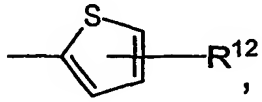
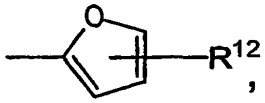







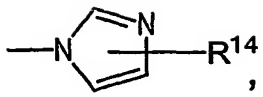
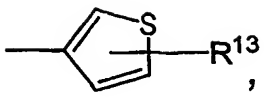
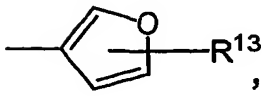
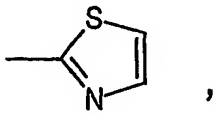
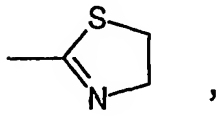
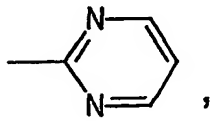
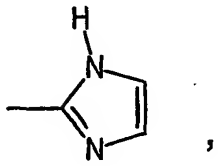
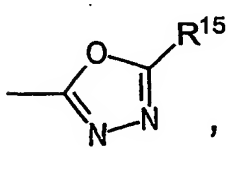
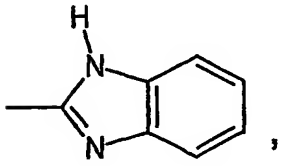
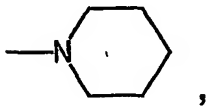
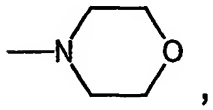
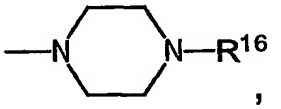
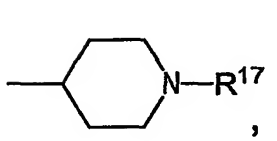
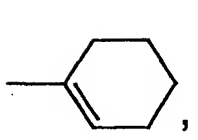
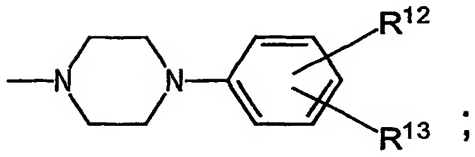
R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other —H, —F, —Cl, —Br, —I, —SO_3H, —SO_3NH_2;

R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$,

—NHR^{16},

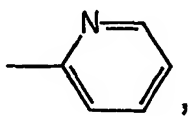
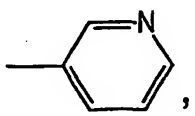
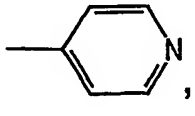
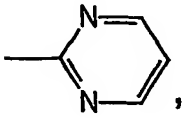
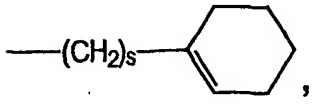
—NHR^{17},

R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$(CH_2)_s$–$COOR^{16}$, —OR^{16}, —SR^{16}, —$NR^{16}R^{17}$, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};

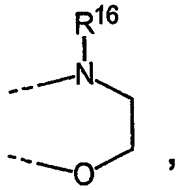
R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —cyclo–C_4H_7, —cyclo–C_3H_5, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —$CH=CH_2$, —CH_2–$CH=CH_2$, —Ph, —CH_2Ph, —$CH(CN)_2$, —CF_3, —CCl_3, —C_2F_5, —$(CH_2)_r$–OH,

m is an integer from 0 – 6,
n is an integer from 0 – 6,

p is an integer from 0 – 6,
q is an integer from 0 – 6,
r is an integer from 1 – 6,
s is an integer from 0 – 6,
and/or their corresponding N-oxides in position 1 and/or 4;
and/or the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and/or pharmaceutically acceptable salts thereof.

3. Compound according to any one of claim 1 or 2 wherein:
R^1 and R^2 are independently of each other —$(CH_2)_p$—NH—$(CH_2)_n$—R^9, —$(CH_2)_s$—S—$(CH_2)_m$—R^{10}, —$(CH_2)_r$—R^3, —CH=CH—R^{11}, —$(CH_2)_q$—R^{11}, —R^9, —R^{10}, —$CH(COOR^{16})(COOR^{17})$, —$CH(CN)(COOR^{16})$,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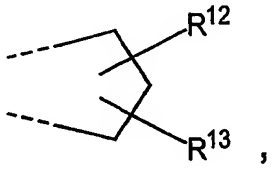
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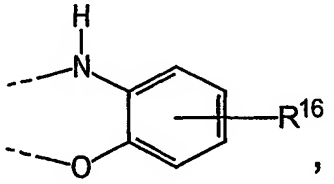
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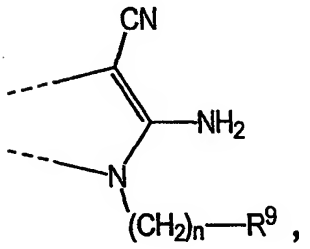
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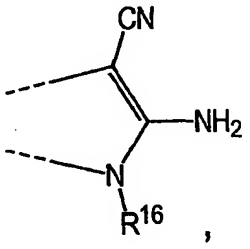
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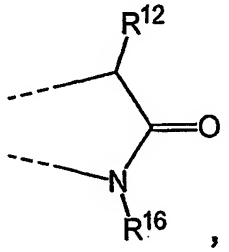
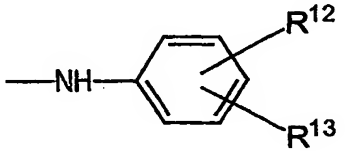

,

R^3, R^4, R^5, R^6, R^7, and R^8 are independently of each other —H, —F, —Cl, —Br, —I, —SO_3H;

R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$,
—NHR^{16},
—NHR^{17},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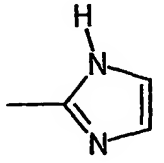
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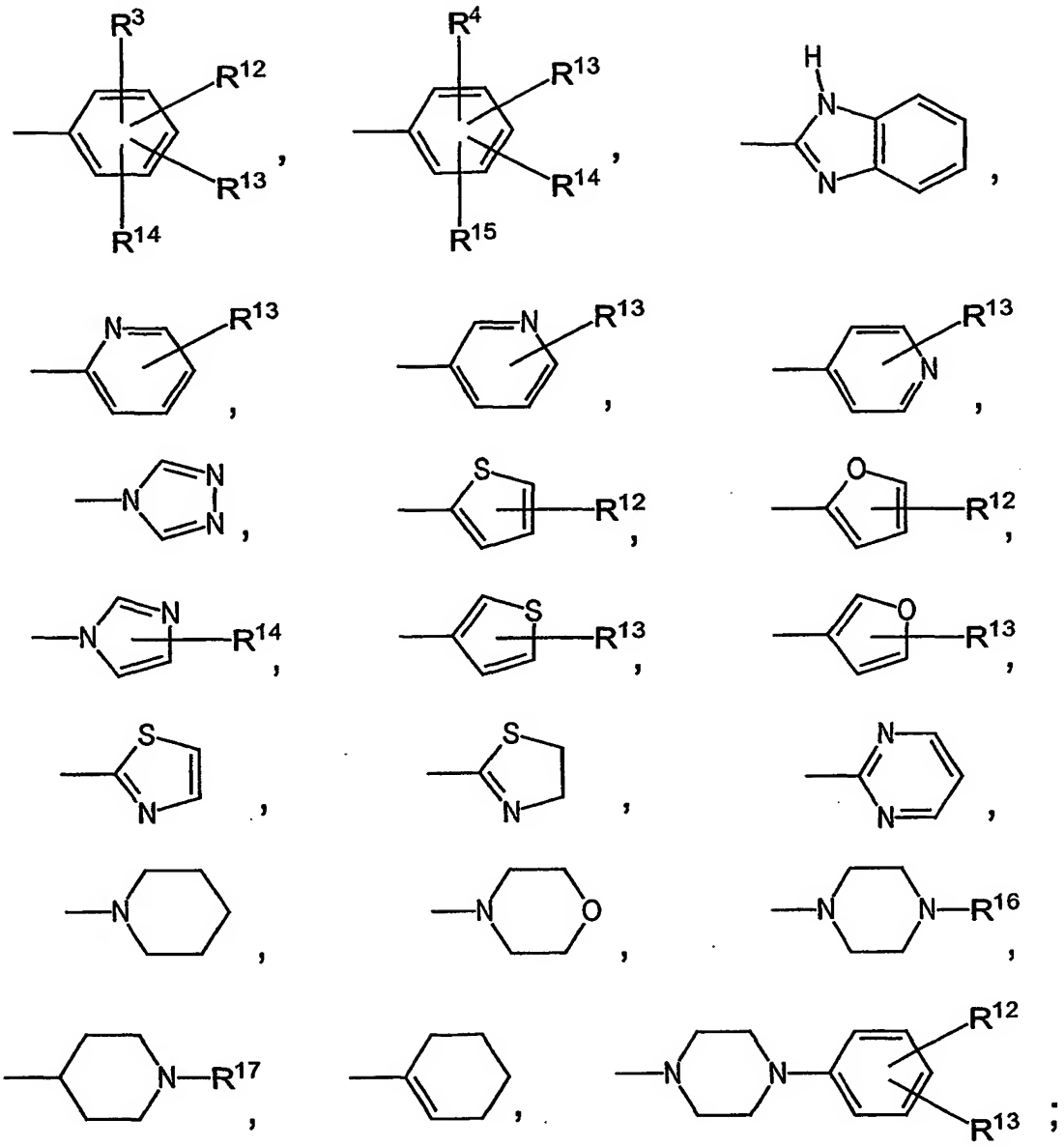
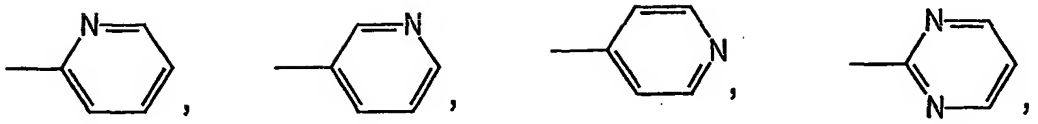


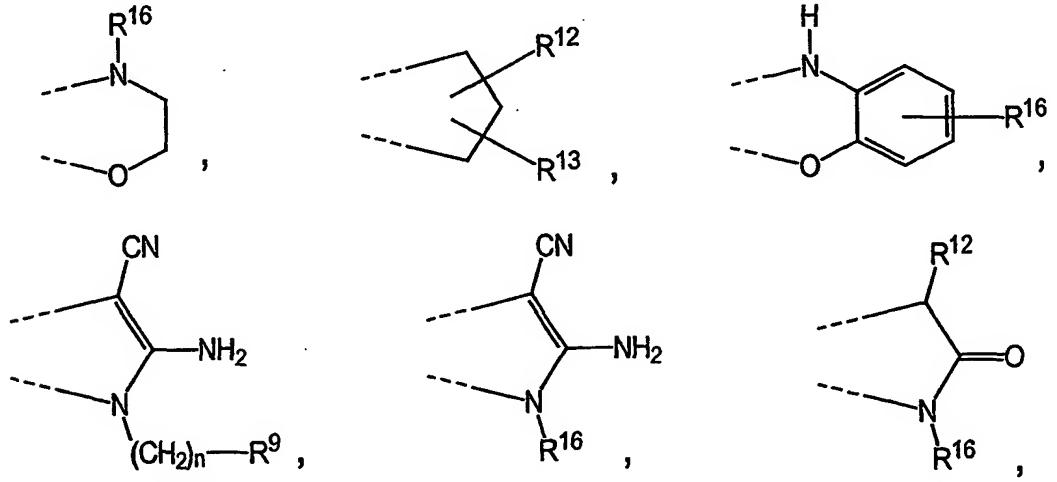
R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$(CH_2)_s$–$COOR^{16}$, —OR^{16}, —SR^{16}, —$NR^{16}R^{17}$, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};

R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —$(CH_2)_r$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —CH_2–CH=CH_2, —Ph, —CH_2Ph, —$CH(CN)_2$, —CF_3, —$(CH_2)_r$–OH,



m is an integer from 0 – 6,
n is an integer from 0 – 6,
p is an integer from 0 – 6,
q is an integer from 0 – 6,
r is an integer from 1 – 6,
s is an integer from 0 – 6,
and/or their corresponding N-oxides in position 1 and/or 4;
and/or the corresponding reduced forms of these compounds wherein the double bond in position 1 and/or 3 is hydrogenated;
and/or pharmaceutically acceptable salts thereof.

4. Compound according to any one of claims 1 – 3 wherein:
R^1 and R^2 are independently of each other —NH—$(CH_2)_n$—R^9, —S—$(CH_2)_m$—R^{10}, —$(CH_2)_p$—NH—R^9, —$(CH_2)_s$—S—R^{10}, —CH_2—R^3, —$(CH_2)_2$—R^3, —$(CH_2)_3$—R^3, —CH=CH—R^{11}, —CH_2—R^{11}, —$(CH_2)_2$—R^{11}, —$(CH_2)_3$—R^{11}, —CH_2—CH(OH)—R^{11}, —R^9, —R^{10}, —$CH(COOR^{16})(COOR^{17})$, —$CH(CN)(COOR^{16})$,

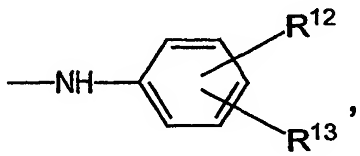


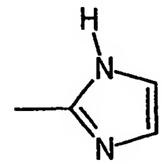
R^3, R^9, R^{10}, R^{11}, R^{16}, R^{17} have the meaning as defined above,
m is an integer from 0 – 4,
n is an integer from 0 – 4,
p is an integer from 0 – 4,
s is an integer from 0 – 4.

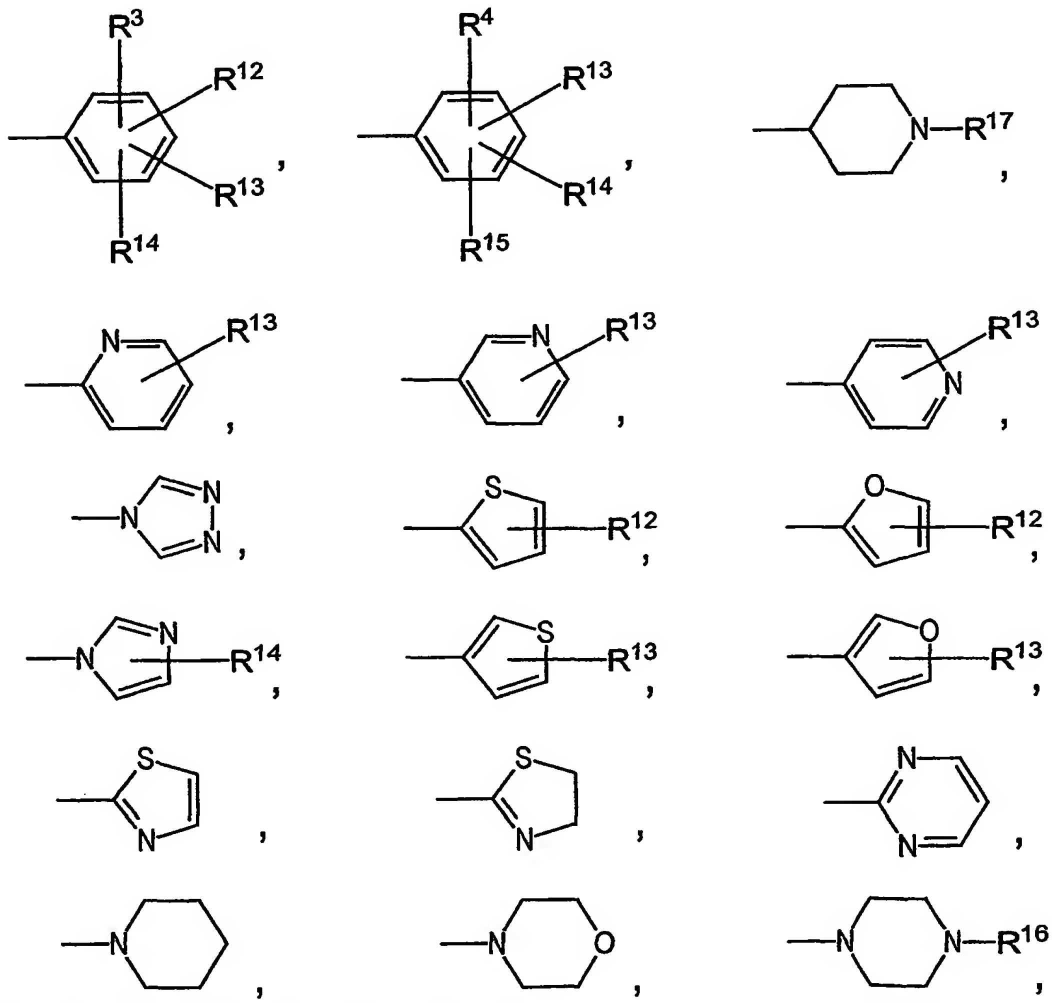
5. Compound according to any one of claims 1 – 4 wherein:
R^9, R^{10}, and R^{11} are independently of each other —CN, —$NR^{16}R^{17}$,

—NHR^{16},

—NHR^{17},





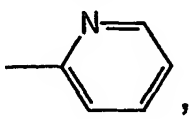


R^3, R^4, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17} have the meaning as defined above.

6. Compound according to any one of claims 1 – 5 wherein:
R^{12}, R^{13}, R^{14}, and R^{15} are independently of each other —R^3, —R^4, —R^5, —R^6, —R^{16}, —R^{17}, —$COOR^{16}$, —CH_2–$COOR^{16}$, —$(CH_2)_2$–$COOR^{16}$, —$(CH_2)_3$–$COOR^{16}$, —OR^{16}, —SR^{16}, —NHR^{17}, —$OOCR^{16}$, —NH–CO–R^{16}, —CO–NH–R^{16}, —CO–R^{17};

R^3, R^4, R^5, R^6, R^{16}, R^{17} have the meaning as defined above.

7. Compound according to any one of claims 1 – 6 wherein:
R^{16} and R^{17} are independently of each other —H, —CH_3, —C_2H_5, —C_3H_7, —$CH(CH_3)_2$, —C_4H_9, —C_5H_{11}, —C_6H_{13}, —cyclo–C_6H_{11}, —cyclo–C_5H_9, —CH_2–$CH(CH_3)_2$, —$(CH_2)_2$–$CH(CH_3)_2$, —$(CH_2)_3$–$CH(CH_3)_2$, —$CH(CH_3)C_2H_5$, —$C(CH_3)_3$, —CH_2–$CH=CH_2$, —Ph, —CH_2Ph, —CF_3, —$CH(CN)_2$, —CH_2–OH, —$(CH_2)_2$–OH, —$(CH_2)_3$–OH, —$(CH_2)_4$–OH,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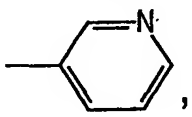
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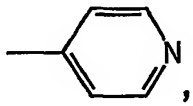
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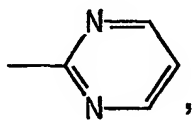
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8. Compound according to any one of claims 1 – 7, wherein R^3 to R^8 represent hydrogen.

9. Compound according to claim 1, wherein the compound is selected from the group comprising:
2-Chloro-benzo[g]quinoxaline
2-(2-Thienyl)-3-chloro-benzo[g]quinoxaline
2,3-Dichloro-benzo[g]quinoxaline
2,3-Bis-(2-thienyl)-benzo[g]quinoxaline
2-Phenyl-benzo[g]quinoxaline
2-para-Tolylbenzo[g]quinoxaline
2-(3-Chlorophenyl)-benzo[g]quinoxaline
2-(4-Chlorophenyl)-benzo[g]quinoxaline
2-(4-Bromophenyl)-benzo[g]quinoxaline
2-Adamantan-2-yl-benzo[g]quinoxaline
2,3-Dipyridyl-2-yl-benzo[g]quinoxaline
2,3-Diphenylbenzo[g]quinoxaline
2,3-Di-para-tolyl-benzo[g]quinoxaline
2,3-Bis-(5-bromo-2-hydroxyphenyl)-benzo[g]quinoxaline
2,3-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline
2,3-Bis-(bromomethyl)-benzo[g]quinoxaline
2,3-Difuran-2-yl-benzo[g]quinoxaline
2,3-Bis-(4-fluorophenyl)-benzo[g]quinoxaline
2-Thiophen-3-yl-3-thiophen-2-yl-benzo[g]quinoxaline

2,3-Bis-(thiophen-3-yl)-benzo[g]quinoxaline
2,3-Dihydro-1H-benzo[g]cyclopenta[b]quinoxaline-1,3-dicarboxylic acid diethyl ester
2-(3,4-Dimethoxyphenyl)-benzo[g]quinoxaline
2-(3,4-Dihydroxyphenyl)-benzo[g]quinoxaline
2-Methyl-3-thiophen-2-yl-benzo[g]quinoxaline
2-Methyl-3-thiophen-2-yl-1,2-dihydro-benzo[g]-quinoxaline
{5-[3-(4-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
{5-[3-(5-Methoxycarbonylmethyl-thiophen-2-ylbenzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
2,3-Bis-(2-methoxycarbonylethyl-thiophen-5-yl)-benzo[g]-quinoxaline
2,3-Bis-(2-ethoxycarbonylpropyl-thiophen-5-yl)-benzo[g]-quinoxaline
{5-[3-(4-Carboxymethyl-thiophen-2-yl)-benzo[g]-quinoxalin-2-yl]-thiophen-3-yl}-acetic acid
2,3-Bis-(2-carboxymethyl-thiophen-5-yl)-benzo[g]-quinoxaline
2,3-Bis-(2-carboxypropyl-thiophen-5-yl)-benzo[g]-quinoxaline
2,3-Bis-(2-carboxyethyl-thiophen-5-yl)-benzo[g]-quinoxaline
{5-[5,10-Dibromo-3-(4-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-3-yl}-acetic acid
{5-[5,10-Dibromo-3-(5-carboxylmethyl-thiophen-2-yl)-benzo[g]quinoxalin-2-yl]-thiophen-3-yl}-acetic acid
2,3-Bis(4-pyridin-2-yl-piperazin-1-ylmethyl)-benzo[g]-quinoxaline hydrochloride
2,3-Bis[4-(4-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(2-methoxyphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(3-trifluoromethylphenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(pyrimidin-2-yl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(3-chlorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(4-nitrophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride
2,3-Bis[4-(2-fluorophenyl)-piperazin-1-ylmethyl)-benzo[g]quinoxaline hydrochloride

2,3-Bis-piperidin-1-ylmethyl-benzo[g]quinoxaline hydrochloride
2,3-Bis-morpholin-4-ylmethyl-benzo[g]quinoxaline hydrochloride
2,3-Bis-(phenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(4-methylphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(4-methoxyphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2,5-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2,6-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(3,4-dichlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2,4-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2,5-dimethylphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2,3,5,6-tetrafluorophenylsulfanylmethyl)-benzo[g]-quinoxaline
2,3-Bis-(2-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(3-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(4-chlorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2-bromophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(3-bromophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(4-fluorophenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(2-methylphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(3-methylphenylsulfanylmethyl)-benzo[g]quinoxaline
2,3-Bis-(4,5-dihydro-thiazol-2-yl-sulfanylmethyl)-benzo[g]-quinoxaline
2,3-Bis-(1H-benzoimidazol-2-ylsulfanylmethyl)-benzo[g]quinoxaline
(3-Methoxycarbonylmethylsulfanylmethyl-benzo[g]-quinoxalin-2-ylmethylsulfanyl)-acetic acid methyl ester
2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malononitrile
2-(3-Chloro-benzo[g]quinoxalin-2-yl)-malonic acid diethyl ester
(3-Chloro-benzo[g]quinoxalin-2-yl)-cyano-acetic acid ethyl ester
2-(3-Chloro-benzo[g]quinoxalin-2-yl)-2-cyano-N-(4-trifluoromethyl-phenyl)-acetamide
N-(3,5-Bis-trifluoromethyl-phenyl)-2-(3-chloro-benzo[g]quinoxalin-2-yl)-2-cyano-acetamide
Benzo[g]quinoxalin-2-yl-(2-ethoxycarbonylphenyl)-amine
4-(Benzo[g]quinoxalin-2-ylamino)-benzenesulfonamide
Benzo[g]quinoxalin-2-yl-(3,4-dimethylphenyl)-amine
Benzo[g]quinoxalin-2-yl-[3,5-bis-(ethoxycarbonyl)-phenyl] amine
Benzo[g]quinoxalin-2-yl-(2-hydroxy-4-methylphenyl)-amine
Benzo[g]quinoxaline-2-yl-phenylamine
Benzo[g]quinoxalin-2-yl-biphenyl-4-yl-amine

Benzo[g]quinoxalin-2-yl-(4-methylphenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-phenoxyphenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-bromophenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-methylsulfanylphenyl)-amine
[4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-phenylmethanone
Benzo[g]quinoxalin-2-yl-(2,4-dimethoxyphenyl)-amine
Benzo[g]quinoxalin-2-yl-(2-hydroxy-5-chlorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(3-fluoro-4-methylphenyl)-amine
Benzo[g]quinoxalin-2-yl-[2-(2-chlorophenyl)-ethyl]-amine
Benzo[g]quinoxalin-2-yl-(3-bromophenyl)-amine
Benzo[g]quinoxaline-2-yl-(3,4-dimethoxyphenyl)-amine
4-(Benzo[g]quinoxaline-2-yl-amino)-benzene-1,2-diol
N-Benzo[g]quinoxalin-2-yl-N'-(4-fluorophenyl)-hydrazine
N-Benzo[g]quinoxalin-2-yl-N'-(2,4-dichlorophenyl)-hydrazine
N-Benzo[g]quinoxalin-2-yl-N'-(3-chlorophenyl)-hydrazine
N-Benzo[g]quinoxalin-2-yl-N'-(4-chlorophenyl)-hydrazine
1-(2-Nitrophenyl)-2-(3-thiophen-2-yl-benzo[g]quinoxaline-2-yl)-ethanol
Benzo[g]quinoxalin-2-yl-(4-ethylphenyl)-amine
N-[4-(Benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide
Benzo[g]quinoxalin-2-yl-(3-chlorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-chlorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(3-fluorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(2-fluorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(2,4-dichlorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-hydroxyphenyl)-amine
Benzo[g]quinoxalin-2-yl-(3-iodophenyl)-amine
Benzo[g]quinoxalin-2-yl-(3,4-dichlorophenyl)-amine
Benzo[g]quinoxalin-2-yl-(3-trifluoromethylphenyl)-amine
Benzo[g]quinoxalin-2-yl-(4-trifluoromethylphenyl)-amine
(5-Chloro-2-methylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine
(2-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(4-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]-quinoxalin-2-yl)-amine
(3,4-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(2,5-Dimethoxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(4-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(3-Fluorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(3-Hydroxyphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine

N-[4-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl-amino)-phenyl]-acetamide
(2-Hydroxy-4-methylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(3-Chlorophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(4-Bromophenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(3-Trifluoromethylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
(2-Morpholin-4-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine
[3-(4-Methylpiperazin-1-yl)-propyl]-(3-thiophen-2-yl-benzo[g]-quinoxalin-2-yl)-amine
(2-Piperidin-1-yl-ethyl)-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-amine
N-(3-Bromophenyl)-N'-(3-thiophen-2-yl-benzo[g]quinoxalin-2-yl)-hydrazine
(4-Butylphenyl)-(3-thiophene-2-yl-benzo[g]quinoxalin-2-yl)-amine
Benzo[g]quinoxalin-2-yl-[2-(2-bromo-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine
Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(3-nitro-phenyl)-2H-pyrazol-3-yl]-amine
Benzo[g]quinoxalin-2-yl-[2-(3-fluoro-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine
Benzo[g]quinoxalin-2-yl-[2-(3-trifluoromethyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine
Benzo[g]quinoxalin-2-yl-[2-(2-methyl-phenyl)-5-tert-butyl-2H-pyrazol-3-yl]-amine
Benzo[g]quinoxalin-2-yl-[5-tert-butyl-2-(4-nitro-phenyl)-2H-pyrazol-3-yl]-amine
[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-(3-chloro-benzo[g]-quinoxalin-2-yl)-amine
[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine
[5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine
[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-(3-chloro-benzo[g]quinoxalin-2-yl)-amine
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
2-(3-([5-tert-Butyl-2-(3-nitrophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol
2-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol

N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine
3-(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
3-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino])-benzo[g]quinoxalin-2-yl-amino)-propanol
3-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-propanol
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine
2-(3-([5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-ylamino](-benzo[g]quinoxalin-2-yl-amino)-ethanol
N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(4-methoxyphenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
2-[(3-([5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-amino)-benzo[g]quinoxalin-2-yl)-(2-hydroxyethyl)-amino]-ethanol

N-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-N'-pyridin-4-yl-methyl-benzo[g]quinoxaline-2,3-diamine
N-(1-Benzylpiperidin-4-yl-methyl)-N'-[5-tert-Butyl-2-(3-fluorophenyl)-2H-pyrazol-3-yl]-benzo[g]quinoxaline-2,3-diamine
2-(3-([5-tert-Butyl-2-phenyl-2H-pyrazol-3-ylamino]-benzo[g]quinoxalin-2-yl-amino)-ethanol
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine
N-[5-tert-Butyl-2-phenyl-2H-pyrazol-3-yl]-N'-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Dipyridin-3-yl-methyl-benzo[g]quinoxaline-2,3-diamine
N,N'-Diphenyl-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-[1,2,4]triazol-4-yl-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-bromophenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-phenoxyphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3,4-dimethyl-phenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-methylsulfanylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-methoxyphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-chloro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-bromophenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-fluorophenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-chlorophenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-ethylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-butylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-trifluoromethylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3,4-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-fluoro-4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(4-methylphenyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(2,5-dimethoxyphenyl)-benzo[g]quinoxaline-2,3-diamine.
N-{4-[3-(4-Acetylaminophenylamino)-benzo[g]quinoxalin-2-yl-amino]-phenyl}-acetamide
N,N'-Bis-(3-methylbutyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(2-hydroxyethyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(5-methylfuran-2-yl-methyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-[2-(3-fluorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-[2-(3-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine

N,N'-Dipyridin-4-yl-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-[2-(4-methoxyphenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-[2-(2-chlorophenyl)-ethyl]-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(2-cyclohex-1-enyl-ethyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(1-benzylpiperidin-4-yl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-imidazol-1-yl-propyl)-benzo[g]quinoxaline-2,3-diamine
N,N'-Bis-(3-hydroxypropyl)-benzo[g]quinoxaline-2,3-diamine
2-Piperidin-1-yl-benzo[g]quinoxaline
1-Benzo[g]quinoxalin-2-yl-piperidine-4-carboxylic acid ethyl ester
2-Morpholin-4-yl-benzo[g]quinoxaline
2-(4-Methyl-piperazin-1-yl)-benzo[g]quinoxaline
4-Benzo[g]quinoxalin-2-yl-piperazine-1-carboxylic acid ethyl ester
2-(4-Phenyl-piperazin-1-yl)-benzo[g]quinoxaline
2-Morpholin-4-yl-3-thiophen-2-yl-benzo[g]quinoxaline
1-(3-Thiophen-2-yl-benzo[g]quinoxalin-2-yl)-piperidine-4-carboxylic acid ethyl ester
2-[4-(4-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
2-[4-(3-Trifluoromethyl-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
2-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
2-(4-Pyridin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline
2-(4-Pyrimidin-2-yl-piperazin-1-yl)-benzo[g]quinoxaline
2-[4-(2-Fluoro-phenyl)-piperazin-1-yl]-benzo[g]quinoxaline
(3-Chloro-benzo[g]quinoxalin-2-yl)-(4-chlorophenyl)-amine
(3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-4-fluoro-phenyl)-amine
(4-Bromo-phenyl)-(3-chloro-benzo[g]quinoxalin-2-yl)-amine
(3-Chloro-benzo[g]quinoxalin-2-yl)-(3-fluoro-phenyl)-amine
(3-Chloro-benzo[g]quinoxalin-2-yl)-(3-chloro-phenyl)-amine
(3-Chloro-benzo[g]quinoxalin-2-yl)-(4-trifluoromethyl-phenyl)-amine
2-(4-Chloro-phenoxy)-benzo[g]quinoxaline
2-(4-Bromo-phenoxy)-benzo[g]quinoxaline
2-(3-Methoxy-phenoxy)-benzo[g]quinoxaline
2-(4-Methoxy-phenoxy)-benzo[g]quinoxaline
2-(3,5-Dimethoxy-phenoxy)-benzo[g]quinoxaline
2-(4-Bromo-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline
2-(4-Chloro-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline
2-(3,5-Dimethoxy-phenoxy)-3-thiophen-2-yl-benzo[g]quinoxaline
2-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxaline
2-(1H-Imidazol-2-yl-sulfanyl)-benzo[g]quinoxaline

2-(1H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]-quinoxaline
2-(Pyrimidin-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]quinoxaline
2-(1H-Imidazol-2-yl-sulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline
2-(2,5-Dichloro-phenylsulfanyl)-3-thiophen-2-yl-benzo[g]-quinoxaline
2-(Pyrimidin-2-yl-sulfanyl)-benzo[g]quinoxaline
4-(3-Chloro-benzo[g]quinoxalin-2-ylsulfanyl)-phenylamine
[5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
[5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
[5-tert-Butyl-2-(3-fluoro-phenyl)-2H-pyrazol-3-yl]-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
[3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-chloro-phenyl)-amine
(3-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
[3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine

[3-(2,4-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(2-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(2-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3-p-Tolylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(4-trifluoromethyl-phenyl)-amine
[3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-trifluoromethyl-phenyl)-amine
[3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(3-Amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(2,4-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(2-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(2-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(3-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine

[3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
(3-Fluorophenyl)-(3-p-toylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
[3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(2,5-Dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
[3-(2,6-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-(3-fluoro-phenyl)-amine
(4-Bromo-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-(3-phenylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
(4-Bromo-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
(4-Bromo-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Bromo-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine

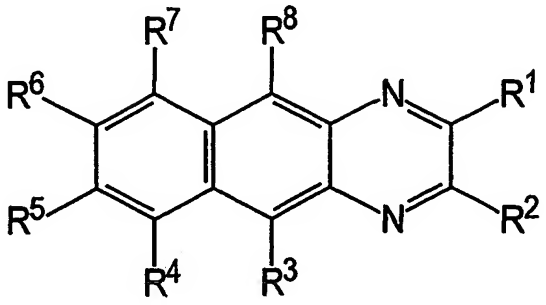
(4-Chloro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(4-Chloro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl)-amine
(4-Chloro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(3-amino-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(2-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(2-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(3-chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-(3-p-tolylsulfanyl-benzo[g]quinoxalin-2-yl]-amine

(3-Chloro-4-fluoro-phenyl)-[3-(3-bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
(3-Chloro-4-fluoro-phenyl)-[3-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxalin-2-yl]-amine
2,3-Bis-(3-chloro-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(naphthalen-2-yl-sulfanyl)-benzo[g]quinoxaline
2,3-Bis-(4-fluoro-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(4-methoxy-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(3,4-dichloro-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(2,5-dichloro-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(3-bromo-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(4-methyl-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(3-methyl-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(5-amino-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]-quinoxaline
2,3-Bis--(5-pyridin-4-yl-[1,3,4]oxadiazol-2-yl-sulfanyl)-benzo[g]-quinoxaline
2,3-Bis-(5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl-sulfanyl)-benzo[g]-quinoxaline
2,3-Bis-(2-methyl-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(2,4-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(3-methoxy-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(2,5-dimethyl-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(4-amino-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(3-amino-phenylsulfanyl)-benzo[g]quinoxaline
2,3-Bis-(1H-imidazol-2-ylsulfanyl)-benzo[g]quinoxaline
4-[3-(3-Chloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
4-[3-(4-Methoxy-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
4-[3-(4-Fluoro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
4-[3-(3,4-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
4-[3-(2,5-Dichloro-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
4-[3-(3-Bromo-phenylsulfanyl)-benzo[g]quinoxalin-2-yl-sulfanyl]-phenylamine
2-Pyridin-4-yl-4,13-dihydro-14-thia-1,3,3a,5,12-pentaaza-azuleno[5,6-b]anthracene
Benzo[g]quinoxaline-6-sulfonic acid sodium salt sodium salt
3-(3,4-Dimethoxy-.phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt

2-Methyl-3-phenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Diphenyl-benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Di-p-tolyl -benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Di-furan-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Dithiophenyl-2-yl-benzo[g]quinoxaline-6-sulfonic acid sodium salt
2,3-Diphenyl-benzo[g]quinoxaline-7-sulfonic acid sodium salt
3-(3,5-Bis-trifluoromethyl-phenyl)-benzo[g]quinoxaline-7-sulfonic acid sodium salt
2,3-Di-thiophen-3-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt
2,3-Di-pyridin-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt
2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-7-sulfonic acid sodium salt
2,3-Bis-(4-bromo-phenyl)-benzo[g]quinoxaline-7-sulfon amide
2,3-Di-thiophen-2-yl-benzo[g]quinoxaline-6-sulfonamide
2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline-6-sulfonamide
5,10-Dibromo-2-(3-chloro-phenyl)-benzo[g]quinoxaline
2-(3,5-Bis-trifluoromethyl-phenyl)-5,10-dibromo-benzo[g]-quinoxaline
5,10-Dibromo-2-(3,4-dimethoxy-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2-methyl-3-phenyl)-benzo[g]-quinoxaline
5,10-Dibromo-2,3-di-thiophen-2-yl-benzo[g]quinoxaline
5,10-Dibromo-2-thiophen-3-yl-3-thiophen-2-yl-benzo [g] –quinoxaline
5,10-Dibromo-2,3-di-thiophen-3-yl-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(5-bromo-2-hydroxy-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2,3-di-furan-2-yl-benzo[g]quinoxaline
5,10-Dibromo-2,3-di-pyridin-2-yl- benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(3-methoxy-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis -phenyl-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(4-methyl-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(4-bromo-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(4-fluoro-phenyl)-benzo[g]quinoxaline
5,10-Dibromo-2,3-bis-(4-methoxy-phenyl)-benzo[g]quinoxaline
{5-[5,10-Dibromo-3-(5-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
{5-[5,10-dibromo-3-(4-methoxycarbonylmethyl-thiophen-2-yl)benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid methyl ester
2,3-Di-thiophen-2-yl-1,2,3,4-tetrahydro-benzo[g]quinoxaline
3-(5-{3-[5-(2-Carboxy-ethyl)-thiophen-2-yl]-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl}-thiophen-2-yl)-propionic acid

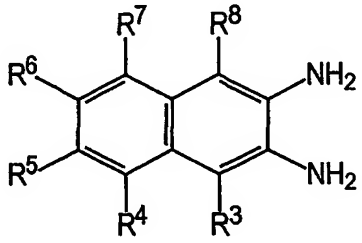
3-Thiophen-2-yl-3,4-dihydro-1H-benzo[g]quinoxalin-2-one
{5-[3-(5-Carboxymethyl-thiophen-2-yl)-1,2,3,4-tetrahydro-benzo[g]quinoxalin-2-yl]-thiophen-2-yl}-acetic acid
3,4-Dihydro-1H-benzo[g]quinoxalin-2-one
2-(3,5-bis-(trifluoromethyl)-phenyl)-benzo[g]quinoxaline-N-oxide
2,3-Bis-(4-fluoro-phenyl)-benzo[g]quinoxaline 1,4-dioxide
2-Amino-1-(2-thiophen-2-yl-ethyl)-1H-benzo[g]pyrrolo[2,3-b] quinoxaline-3-carbonitrile
2-Amino-1-(2-hydroxy-ethyl)-1H-benzo[g]pyrrolo-[2,3-b] -quinoxaline-3-carbonitrile
2-Amino-1-(3-methyl-butyl)-1H-benzo[g]pyrrolo-[2,3-b] -quinoxaline-3-carbonitrile
2-Amino-1-(2-hydroxy-propyl)-1H-benzo[g]pyrrolo-[2,3-b] -quinoxaline-3-carbonitrile
2-Amino-1-[2-(3-fluoro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile
2-Amino-1-[2-(3-chloro-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile
2-Amino-1-[2-(4-methoxy-phenyl)-ethyl]-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile
2-Amino-1-(2-cyclohex-1-enyl-ethyl)-1H-benzo[g]pyrrolo-[2,3-b] quinoxaline-3-carbonitrile
2-Amino-1-(3-imidazol-1-yl-propyl)-1H-benzo[g]pyrrolo-[2,3-b] -quinoxaline-3-carbonitrile
1-(2-Hydroxy-ethyl)-2-oxo-2,3-dihydro-1H-benzo[g]pyrrolo[2,3-b]quinoxaline-3-carboxylic acid ethyl ester
2-(2,3-Dihydro-1-oxa-4,5,12-triaza-naphthacen-4-yl)-ethanol
2-[2-(2,4-Dichlorophenyl)-vinyl]-3-thiophen-2-yl-benzo[g]-quinoxaline
1,2,3,4-Tetrahydrobenzo[b]phenazine
2-(5-Pyridin-4-yl-1H-[1,2,4]triazole-3-ylsulfanyl)-benzo[g]quinoxaline
2-(1H-Benzoimidazole-2-ylsulfanyl)-benzo[g]quinoxaline
2-(4-Nitrophenyl)-benzo[g]quinoxaline
2,3-Dimethyl-benzo[g]quinoxaline
2-Phenyl-3-trifluoromethyl-benzo[g]quinoxaline
2-Methyl-3-phenyl-benzo[g]quinoxaline
2,3-Bis-(4-bromophenyl)-benzo[g]quinoxaline
2-(4-Fluorophenyl)-benzo[g]quinoxaline
and/or pharmaceutically acceptable salts thereof.

10. Process for preparing the compounds having the general formula (I)



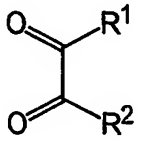
wherein
the substituents R^1 – R^8 have the meanings as defined in claim 1 and/or salts thereof characterized in that

a) a 2,3-diaminonaphthalene compound of the general formula (II)



(II)

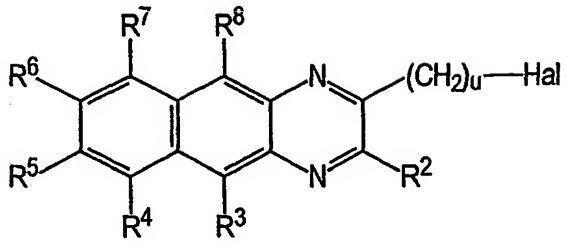
is reacted with a 1,2-diketone of the general formula (III)



(III)

in a polar solvent at an elevated temperature, wherein the substituents R^3 – R^8 in formula (II) and the substituents R^1 – R^2 in formula (III) have the meanings as defined in claim 1; or

b) a halogen-benzo[g]quinoxaline compound of the general formula (IV)



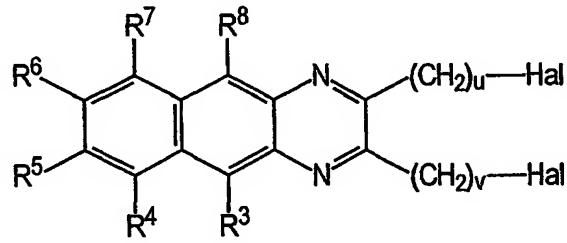
(IV)

wherein Hal represents a halogen selected from —F, —Cl, —Br, —I, and u is an integer from 0 – 6,
is reacted with a nucleophilic compound of the general formula (V)

(V)

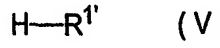
in a polar solvent optionally at elevated reaction temperatures and optionally by the use of a base, wherein the substituents R^2 – R^8 in formula (IV) have the meanings as defined in claim 1 and the substituent —$(CH_2)_u$—$R^{1'}$ has the meaning of R^1 as defined in claim 1; or

c) a dihalogen-benzo[g]quinoxaline compound of the general formula (VI)



(VI)

wherein Hal represents a halogen selected from —F, —Cl, —Br, —I, and u and v are independently of each other an integer from 0 – 6,
is reacted with a nucleophilic compound of the general formula (V)



(V)

in a polar solvent optionally at elevated reaction temperatures and optionally by the use of a base and the obtained product is subsequently reacted with a nucleophilic compound of the general formula (VII)

$$H—R^{2'} \qquad (VII)$$

in a polar solvent optionally at elevated reaction temperatures and optionally by the use of a base, wherein the substituents R^3 – R^8 in formula (VI) have the meanings as defined in claim 1 and the substituent $—(CH_2)_u—R^{1'}$ has the meaning of R^1 as defined in claim 1 and the substituent $—(CH_2)_v—R^{2'}$ has the meaning of R^2 as defined in claim 1.

11. Use of at least one compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts of these compounds as pharmaceutically active agents.

12. Use of a compound according to claim 11 and/or pharmaceutically acceptable salts of these compounds for prophylaxis and/or treatment of infectious diseases including opportunistic diseases.

13. Use of a compound according to claim 11 or 12 and/or pharmaceutically acceptable salts thereof for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of mycobacteria-induced infections, including mycobacteria-induced opportunistic infections.

14. Use of a compound according to any one of claims 11 – 13 and/or pharmaceutically acceptable salts thereof for prophylaxis and/or treatment of mycobacteria-induced infections, including mycobacteria-induced opportunistic infections.

15. Use of a compound according to any one of claims 11 – 14 and/or pharmaceutically acceptable salts thereof as inhibitors for mycobacterial protein kinases.

16. Use according to claim 15, wherein said mycobacterial protein kinase is a serine-threonine protein kinase of *Mycobacterium tuberculosis*.

17. Use according to claim 16, wherein said mycobacterial serine-threonine protein kinase is Pkn A, Pkn B, Pkn D, Pkn E, Pkn F, Pkn G, Pkn H, Pkn I, Pkn J, Pkn K and Pkn L.

18. Use according to any one of claims 13 – 17, wherein the mycobacteria-induced infection or mycobacteria-induced opportunistic infection is tuberculosis, leprosy or mycobacteria-induced meningitis.

19. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of infections and diseases mediated by infections of retroviruses, adenoviruses, hepadnaviruses, herpesviruses, influenza viruses and/or paramyxoviruses.

20. Use according to claim 19, wherein the virus is a retrovirus selected from lentiviruses and oncoretroviruses.

21. Use according to claim 20, wherein the lentivirus is HIV-1, HIV-2, FIV, BIV, SIVs, CAEV, VMV or EIAV.

22. Use according to claim 20, wherein the oncoretrovirus is selected from HTLV-I, HTLV-II or BLV.

23. Use according to claim 19, wherein the paramyxovirus is respiratory syncytial virus.

24. Use according to claim 19, wherein the herpesvirus is selected from Herpes simplex virus I, Herpes simplex virus II, Varicella Zoster virus, Epstein-Barr virus, HCMV, or HHV8.

25. Use according to claim 19, wherein the hepadnavirus is selected from HBV, HCV, GSHV, or WHV.

26. Use according to claims 19 – 25, wherein the virus is a drug resistant virus strain.

27. Use according to claim 21, wherein the virus is a HIV-1 or HIV-2 strain which is resistant against protease inhibitors and/or reverse transcriptase inhibitors.

28. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof as an inhibitor of nuclear export of TNF-α mRNA in TNF-α mediated diseases.

29. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof for prophylaxis and/or treatment of TNF-α mediated diseases.

30. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof as an inhibitor for protein kinases and/or phosphatases.

31. Use according to claim 30, wherein the protein kinase is the herpes viral kinase UL-97.

32. Use according to claim 30, wherein the protein kinase is the human protein kinase SRPK1 and/or SRPK2.

33. Use according to claim 30, wherein the protein kinase is the human protein kinase InsR, Abl, Akt, Adk1, PDGFR, and/or Src.

34. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of a malignant diseases.

35. Use according to claim 34, wherein the malignant disease is selected from the group comprising cancer, epithelial cell-derived tumor, a monocytosis, a basal and squamous cell carcinoma, a hyperproliferating skin disease and psoriasis.

36. Use according to claim 35, wherein the cancer is selected from the group comprising bladder, breast, central nervous system, colon, gastric, lung,

melanoma, head and neck, ovarian, cervix, glioblastoma, prostate, testis, leucemia, liver, and renal cancer.

37. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof as an inhibitor for cellular hyperproliferation of cancer cells.

38. Use of a compound according to any one of claims 1 – 9 and/or pharmaceutically acceptable salts thereof for the manufacture of a pharmaceutical formulation for prophylaxis and/or treatment of diabetes mellitus Type I and/or diabetes mellitus Type II.

39. Use of a compound according to any one of claims 11 – 38 wherein the compound of the general formula (I) and/or pharmaceutically acceptable salts thereof is administered in a dosage corresponding to an effective concentration in the range of 0.01 – 50 µM.

40. Pharmaceutical composition comprising at least one compound according to any one of claims 1 – 9 as an active ingredient and a pharmaceutically acceptable carrier, excipient or diluents.

41. Method for preventing and/or treating infectious diseases, including opportunistic infections in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof, effective to prevent and/or treat said infectious disease.

42. Method according to claim 41, wherein said infectious disease is caused by retroviruses, adenoviruses, hepadnaviruses, herpesviruses, influenza viruses and/or paramyxoviruses.

43. Method according to claim 42, wherein the virus is a retrovirus selected from lentiviruses and oncoretroviruses.

44. Method according to claim 43, wherein the lentivirus is HIV-1, HIV-2, FIV, BIV, SIVs, CAEV, VMV or EIAV.

45. Method according to claim 43, wherein the oncoretrovirus is selected from HTLV-I, HTLV-II or BLV.

46. Method according to claim 42, wherein the paramyxovirus is respiratory syncytial virus.

47. Method according to claim 42, wherein the herpesvirus is selected from Herpes simplex virus I, Herpes simplex virus II, Varicella Zoster virus, Epstein-Barr virus, HCMV, or HHV8.

48. Method according to claim 42, wherein the hepadnavirus is selected from HBV, HCV, GSHV, or WHV.

49. Method according to any one of claims 42 – 48, wherein the virus is a drug resistant virus strain.

50. Method according to claim 44, wherein the virus is a HIV-1 or HIV-2 strain which is resistant against protease inhibitors and/or reverse transcriptase inhibitors.

51. Method for preventing and/or treating CMV in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof effective to inhibit the herpes viral kinase UL-97.

52. Method for preventing and/or treating HBV in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof effective to inhibit the human protein kinase SRPK1 and/or SRPK2.

53. Method for preventing and/or treating diabetes mellitus type I and/or diabetes mellitus type II in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof effective to activate the human protein kinase InsR.

54. Method for preventing and/or treating mycobacteria-induced infections and diseases, including mycobacteria-induced opportunistic infections in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof, effective to prevent and/or treat mycobacteria-induced infections.

55. Method for preventing and/or treating mycobacteria-induced infections and diseases, including mycobacteria-induced opportunistic infections according to claim 54 wherein the mycobacteria-induced infection is tuberculosis, leprosy or mycobacteria-induced meningitis.

56. Method for preventing and/or treating *Mycobacterium tuberculosis* induced infections and diseases, including *Mycobacterium tuberculosis* induced opportunistic infections in an individual comprising the step of administering a pharmaceutically effective amount of a compound according to any one of claims 1 to 9 which inhibits at least partially the activity of the *Mycobacterium tuberculosis* serine-threonine protein kinase Pkn A, Pkn B, Pkn D, Pkn E, Pkn F, Pkn G, Pkn H, Pkn I, Pkn J, Pkn K and Pkn L.

57. Method for preventing and/or treating *Mycobacterium tuberculosis* induced infections and diseases, including *Mycobacterium tuberculosis* induced opportunistic infections in cells comprising the step of administering a pharmaceutically effective amount of a compound according to any one of claims 1 to 9 which inhibits at least partially the activity of the *Mycobacterium tuberculosis* serine-threonine protein kinase Pkn A, Pkn B, Pkn D, Pkn E, Pkn F, Pkn G, Pkn H, Pkn I, Pkn J, Pkn K and Pkn L.

58. Method for down-regulating or inhibiting the growth and/or cell division of *Mycobacterium tuberculosis* in an individual comprising the step of administering a pharmaceutically effective amount of a compound according to any one of claims 1 to 9 which inhibits at least partially the activity of the *Mycobacterium tuberculosis* serine-threonine protein kinase Pkn A, Pkn B, Pkn D, Pkn E, Pkn F, Pkn G, Pkn H, Pkn I, Pkn J, Pkn K and Pkn L.

59. Method for regulating and/or inhibiting of nuclear export of TNF-α mRNA in TNF-α mediated diseases, comprising administering a subject in need

thereof a pharmaceutically effective amount of at least one compound of the general formula (I) and/or pharmaceutically active salts thereof, effective to treat and/or regulate said nuclear export of TNF-α mRNA in TNF-α mediated diseases.

60. Method for prophylaxis and/or treatment of TNF-α mediated diseases, comprising administering a mammal, including a human, in need thereof a pharmaceutically effective amount of at least one compound of the general formula (I) and/or pharmaceutically active salts thereof, effective to treat and/or prevent said TNF-α mediated diseases.

61. Method for preventing and/or treating malignant diseases in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof effective to prevent and/or treat said malignant disease.

62. Method according to claim 61, wherein said malignant disease is selected from the group comprising cancer, epithelial cell-derived tumor, a monocytosis, a basal and squamous cell carcinoma, a hyperproliferating skin disease and psoriasis.

63. Method according to claim 62, wherein the cancer is selected from the group comprising bladder, breast, central nervous system, colon, gastric, lung, melanoma, head and neck, ovarian, cervix, glioblastoma, prostate, testis, leucemia, liver, and renal cancer.

64. Method for inhibiting cellular hyperproliferation of cancer cells, comprising administering a subject in need thereof a pharmaceutically effective amount of at least one compound of the general formula (I) and/or pharmaceutically active salts thereof, effective to inhibit said cellular hyperproliferation of cancer cells.

65. Method for preventing and/or treating cancer in a mammal, including a human, which comprises administering to the mammal an amount of at least one compound of claims 1 to 9 and/or pharmaceutically acceptable salts thereof effective to inhibit at least partially one of the human protein kinases Abl, Akt, Adk1, PDGFR, and/or Src.

66. Method according to any one of claims 41 – 65 wherein the compound of the general formula (I) and/or pharmaceutically acceptable salts thereof is administered in a dosage corresponding to an effective concentration in the range of 0.01 – 50 µM.

67. Method for identifying compounds useful for the prophylaxis and/or treatment of HBV infections and/or diseases comprising:
a) contacting a test compound with the human cellular protein kinase SRPK1 and/or SRPK2; and
b) detecting the activity of said human cellular protein kinase.

68. A monoclonal or polyclonal antibody that binds to the human cellular protein kinase SRPK1 and/or SRPK2.

69. Method for preventing and/or treating HBV infections and/or diseases in an individual comprising the step of administering a pharmaceutically effective amount of an agent which inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or which inhibits at least partially the production of the human cellular protein kinase SRPK1 and/or SRPK2.

70. Method for regulating the production and/or replication of HBV in an individual comprising the step of administering an individual a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or wherein said agent at least partially inhibits the production of the human cellular protein kinase SRPK1 and/or SRPK2.

71. Method for regulating the production and/or replication of HBV in cells comprising the step of administering the cells a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2, or wherein said agent at least partially inhibits the production of the human cellular protein kinase SRPK1 and/or SRPK2.

72. Method according to claim 69, 70, or 71 wherein the agent is a monoclonal or polyclonal antibody which binds to a human cellular protein kinase SRPK1 and/or SRPK2.

73. Method according to claim 69, 70, or 71 wherein the agent is at least one compound according to any one of claims 1 to 9 which inhibits at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2.

74. Oligonucleotide that binds to the DNA or RNA encoding the human cellular protein kinase SRPK1 and/or SRPK2.

75. Method for regulating the expression of the human cellular protein kinase SRPK1 and/or SRPK2 in an individual comprising the step of administering the individual a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the transcription of DNA or the translation of RNA encoding SRPK1 or SRPK2.

76. Method for regulating the expression of the human cellular protein kinase SRPK1 and/or SRPK2 in cells comprising the step of administering the cells a pharmaceutically effective amount of an agent wherein said agent inhibits at least partially the transcription of DNA or the translation of RNA encoding SRPK1 or SRPK2.

77. Method according to claim 69, 70, 71, 75 or 76 wherein the agent is a oligonucleotide which binds to the DNA and/or RNA encoding fully or at least partially the human cellular protein kinase SRPK1 and/or SRPK2.

78. A solid support useful for screening compounds useful for the prophylaxis and/or treatment of HBV infections and/or diseases in an individual, the solid support comprising at least one immobilized oligonucleotide, wherein said oligonucleotide encodes the human cellular protein kinase SRPK1 and/or SRPK2.

79. A solid support useful for screening compounds useful for the prophylaxis and/or treatment of HBV infections and/or diseases in an individual, the solid support comprising the immobilized human cellular protein kinase SRPK1 and/or SRPK2.

80. Pharmaceutical composition useful for the prophylaxis and/or treatment of an individual afflicted with HBV comprising at least one agent capable of inhibiting at least partially the activity of the human cellular protein kinase SRPK1 and/or SRPK2.

81. Pharmaceutical composition according to claim 13 further comprising at least one therapeutic compound selected from the group of hepatitis B virus drugs or vaccines comprising lamivudine, Zeffix®, Heptovir®, 3TC®, Epivir-HBV, Combivir®, Trizivir®, alpha interferon, Intron A®, FTC, Coviracil®, DAPD, DXG, L-FMAU, Clevudine®, Adefovir dipivoxil, tenofovir, epavudine, epcitabine, lobucavir, Penciclovir, Entecavir/BMS-200475, Racivir, L-ddA prodrug, HDP-P-acyclovir, ara-AMP prodrugs, thymosin alpha-1, Zadaxin®, (-)-Carbovir, hammerhead ribozymes, HBV DNA vaccine, Genevax®, PreS1/S2 vaccine, Hepagene®, HBV immunoglobulin, Nabi-HBV®, glycosidase inhibitors, Nonyl-DNJ, human monoclonal antibodies directed against HBV.

82. Pharmaceutical composition according to claim 80 or 81, wherein said agent is at least one compound according to any one of claims 1 to 9.

Figure 1

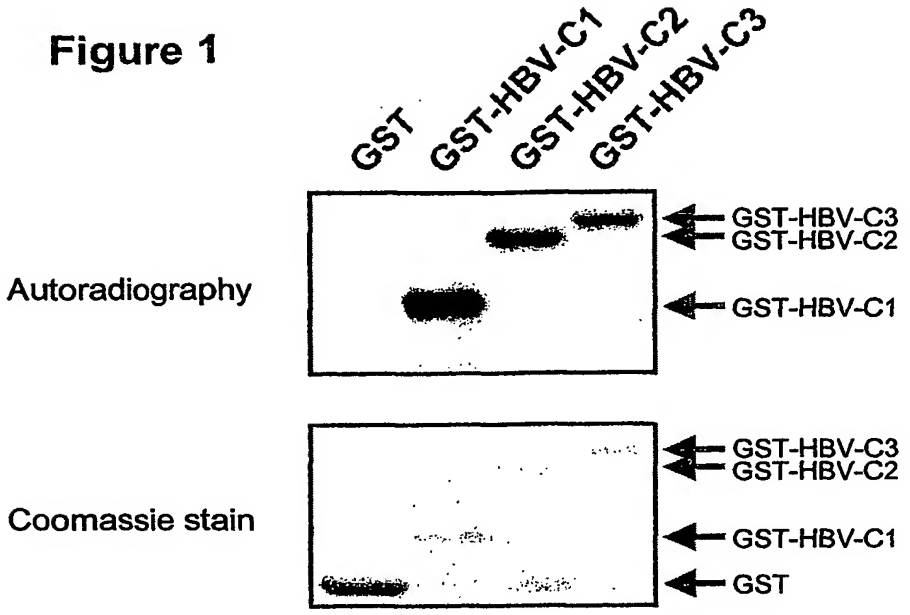


Figure 2

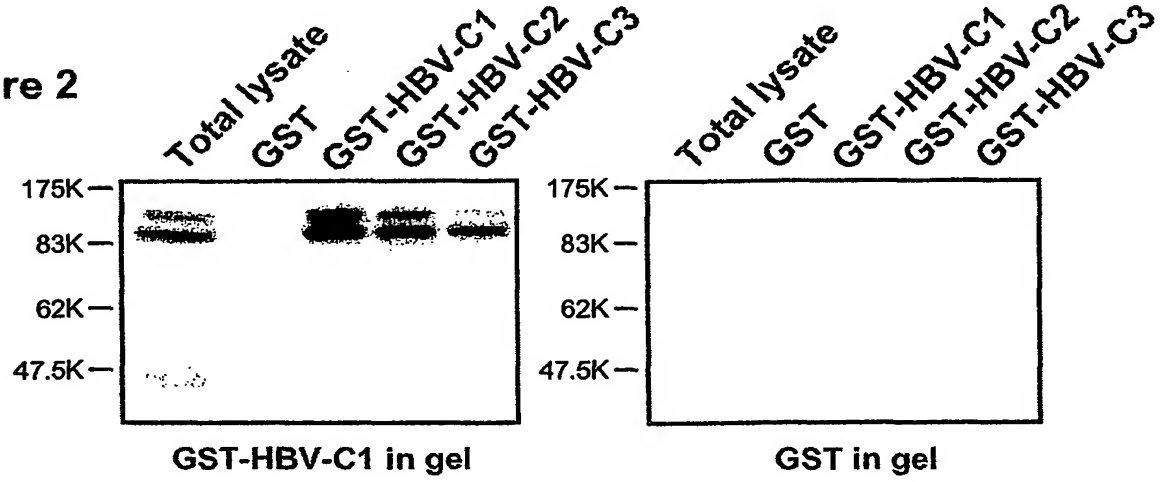


Figure 3

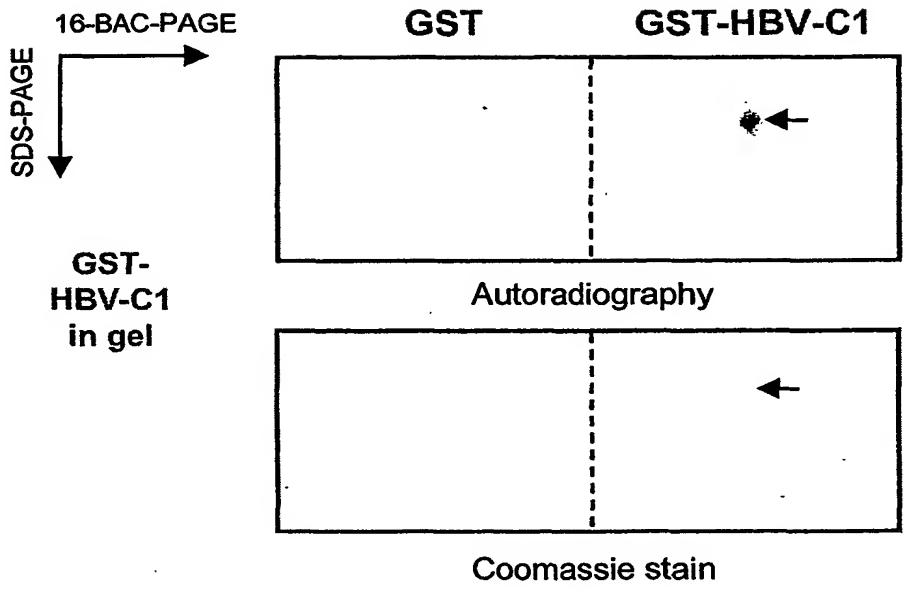

16-BAC-PAGE
SDS-PAGE
GST-
HBV-C1
in gel
GST
GST-HBV-C1
Autoradiography
Coomassie stain

Figure 4

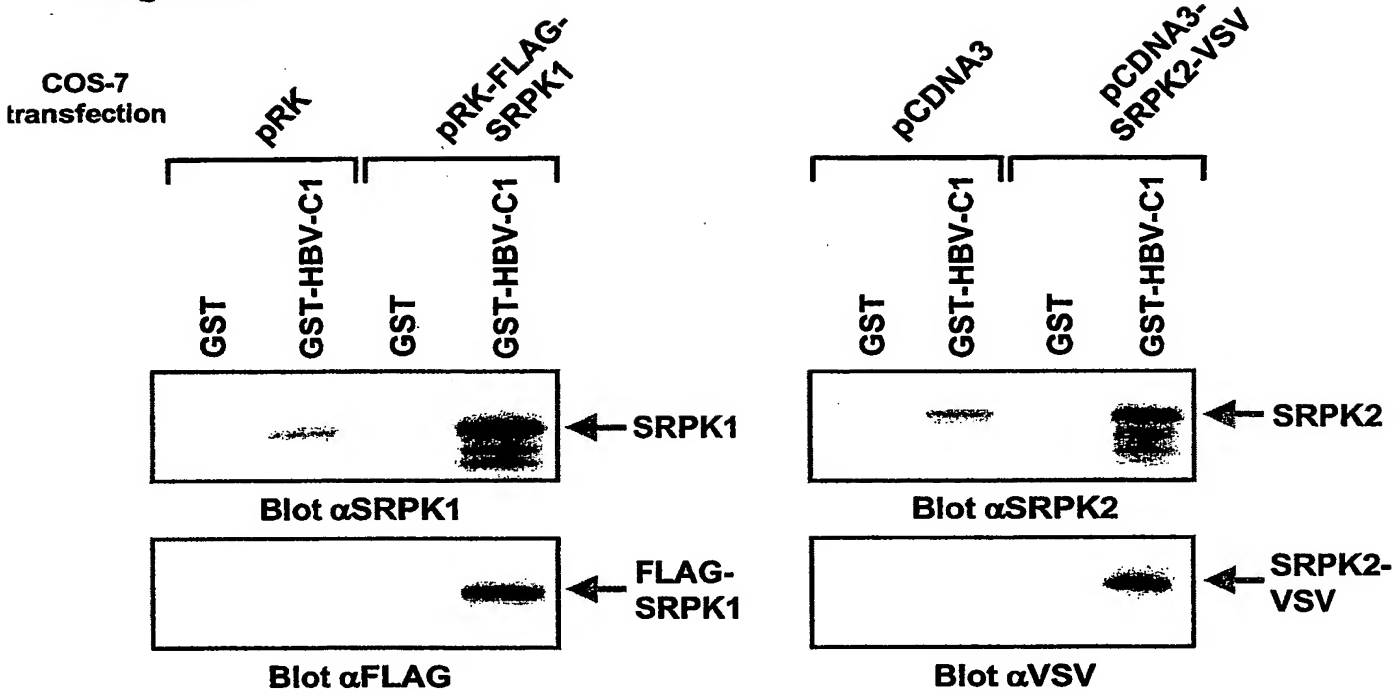


Figure 5

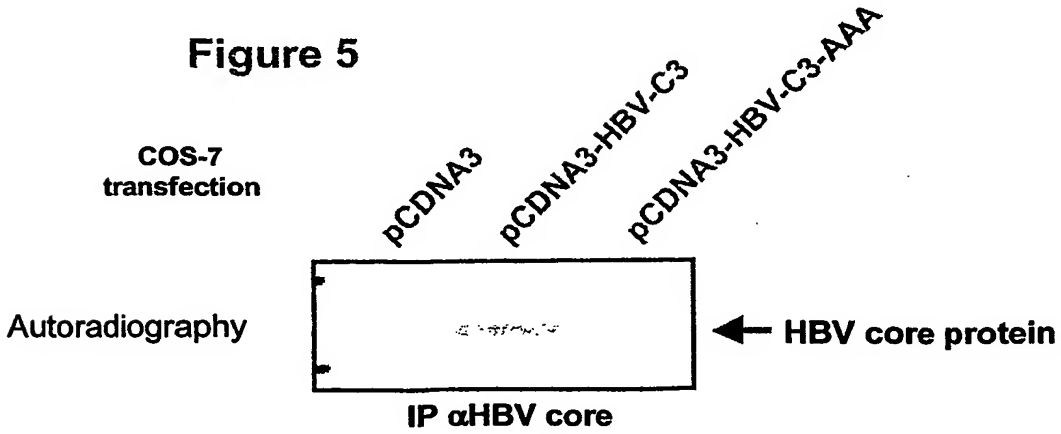
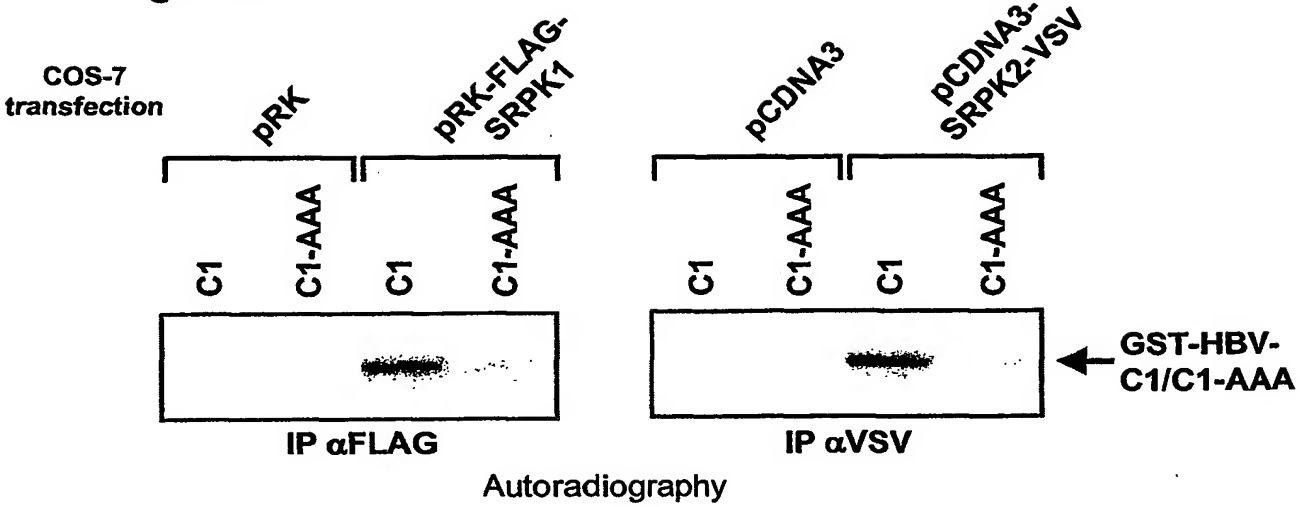


Figure 6



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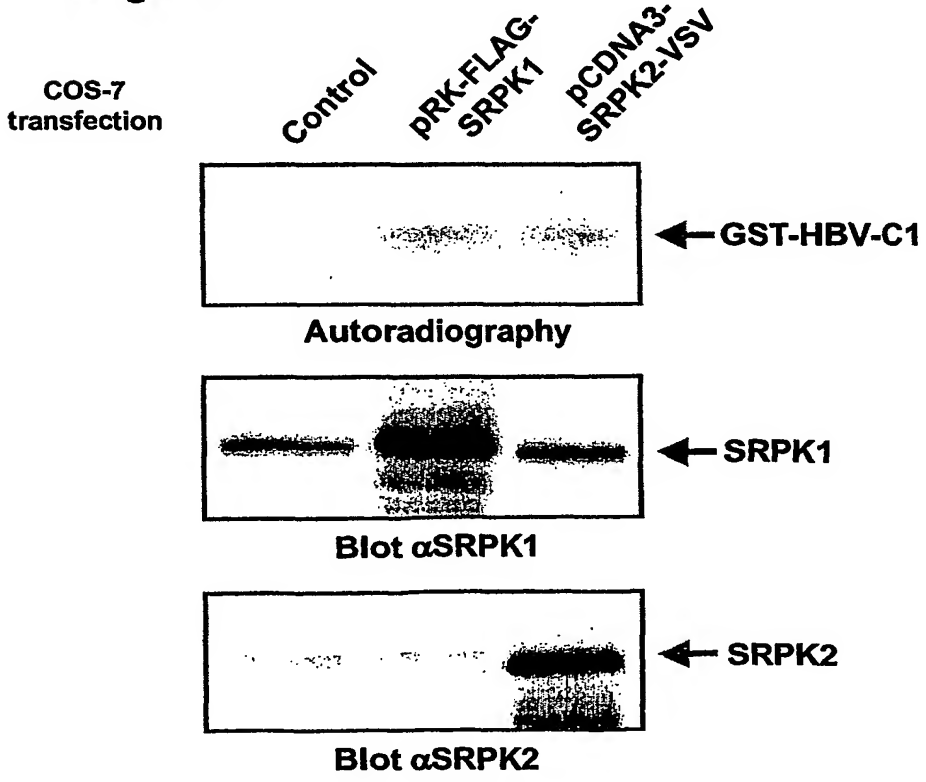
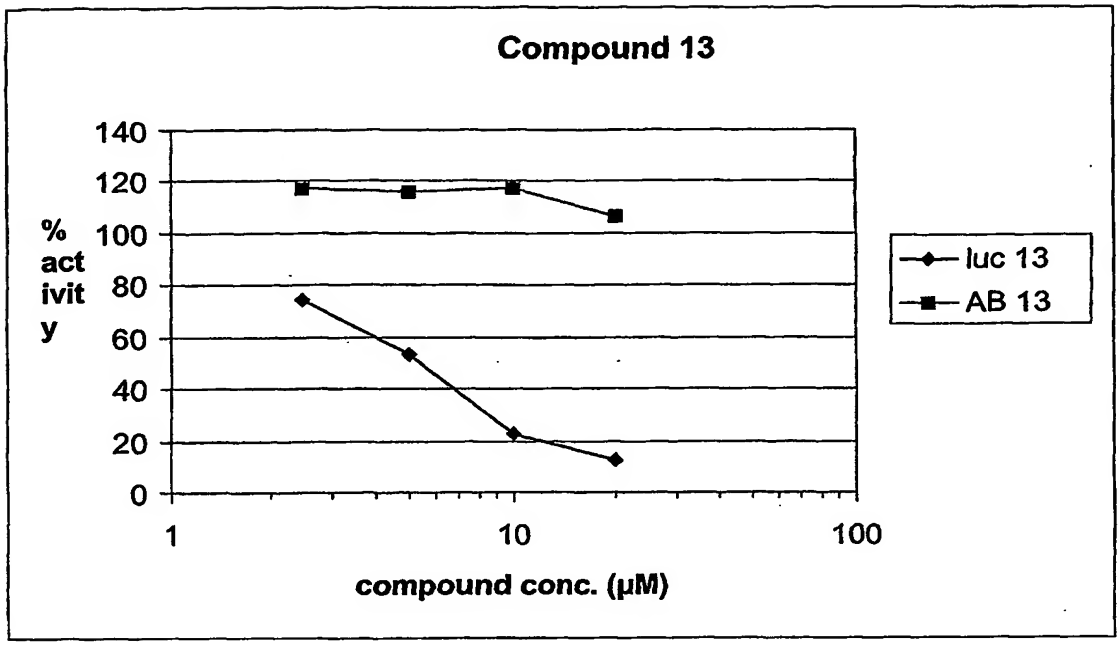


Fig. 8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60
40
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% activity
1
10
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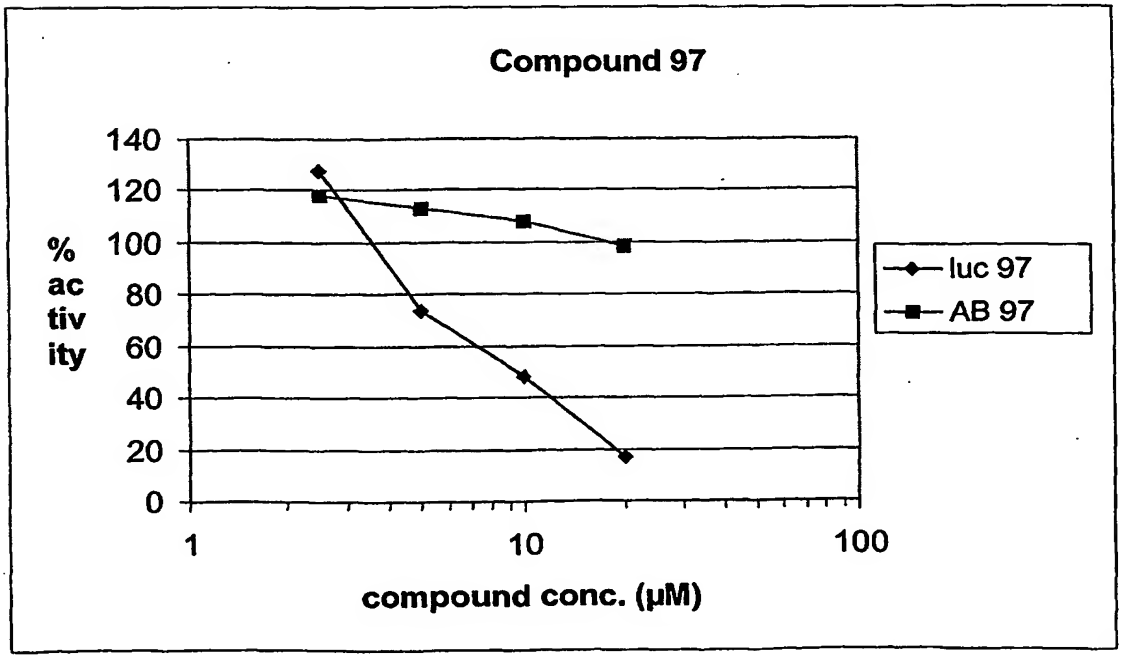
compound conc. (µM)
luc 13
AB 13

Fig. 9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<120> Benzo[g]quinoxaline derivatives as effective compounds against infectious diseases

<130> AXX-P11016-WO

<140>
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<150> US 60/298,902
<151> 2001-06-19

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Tyr Ser Met Gly Asp Thr Met Ser Glu Ser Ala Gly Asp Thr
50 55 60
Phe Gln Gln Tyr Gly Tyr His Gly Ile Phe Arg Gly Arg Asn Leu Trp
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Gln Lys Leu Lys Val Leu Asn Ile Thr Leu Lys Gln His
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100 105 110
Gln Ile Glu Lys Trp Leu Phe Asn Tyr Met Thr Leu Lys Tyr Gln
115 120 125
Glu Leu Met Glu His Ile Ser Ala Trp Tyr Leu Lys Phe Trp Gly Ile
130 135 140
Ile Cys Ser Ser Gly Ser Ser Asn Pro Ile Ile Arg Gly Phe His Cys
145 150 155 160
Leu Val Ser Lys Lys Leu Phe Ser Lys Cys Tyr Arg Val Leu Ile Ile
165 170 175
Tyr Ile Pro Ser Ala Val Ser Ser Thr Leu Thr Leu Asn Gln Arg Thr
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Gly Lys Lys Asp Gln Thr Ser Lys Lys Asn Gln Arg Val Leu Leu Lys
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Asp Pro Lys Arg Thr His Leu Ile Lys Pro Lys Lys Asn Leu
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Lys Ser Gln Val Pro Leu Ala Arg Ile Lys Arg Leu Trp Asn Val Ile
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Pro Arg Asn Phe Ser Pro Lys Lys Val Thr     Asn Ile Ser Arg Ser
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Leu Arg Lys Arg Gln Leu Ala Ser Gln Ile Ser Tyr Cys Pro Cys Trp
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Ser     Ser Leu Arg Arg Glu Pro Leu Pro Pro Ser Val Ser Gly Thr
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35 40 45
Ile Leu Gly Ser Asp Asp Glu Glu Gln Glu Asp Pro Ala Asp Tyr Cys
50 55 60
Lys Gly Gly Tyr His Pro Val Lys Ile Gly Asp Leu Phe Asn Gly Arg
65 70 75 80
Tyr His Val Ile Arg Lys Leu Gly Trp Gly His Phe Ser Thr Val Trp
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Phe Pro Glu Phe Ser Thr Ser Leu Phe Ser Gly Ser Leu Glu Pro Val
    450                 455                 460
```

Ala Cys Gly Ser Val Leu Ser Glu Gly Ser Pro Leu Thr Glu Gln Glu
465 470 475 480
Glu Ser Ser Pro Ser His Asp Arg Ser Arg Thr Val Ser Ala Ser Ser
485 490 495
Thr Gly Asp Leu Pro Lys Ala Lys Thr Arg Ala Ala Asp Leu Leu Val
500 505 510
Asn Pro Leu Asp Pro Arg Asn Arg Asp Lys Ile Arg Val Lys Ile Ala
515 520 525
Asp Leu Gly Asn Ala Cys Trp Val His Lys His Phe Thr Glu Asp Ile
530 535 540
Gln Thr Arg Gln Tyr Arg Ser Ile Glu Val Leu Ile Gly Ala Gly Tyr
545 550 555 560
Ser Thr Pro Ala Asp Ile Trp Ser Thr Ala Cys Met Ala Phe Glu Leu
565 570 575
Ala Thr Gly Asp Tyr Leu Phe Glu Pro His Ser Gly Glu Asp Tyr Ser
580 585 590
Arg Asp Glu Asp His Ile Ala His Ile Ile Glu Leu Leu Gly Ser Ile
595 600 605
Pro Arg His Phe Ala Leu Ser Gly Lys Tyr Ser Arg Glu Phe Phe Asn
610 615 620
Arg Arg Gly Glu Leu Arg His Ile Thr Lys Leu Lys Pro Trp Ser Leu
625 630 635 640
Phe Asp Val Leu Val Glu Lys Tyr Gly Trp Pro His Glu Asp Ala Ala
645 650 655
Gln Phe Thr Asp Phe Leu Ile Pro Met Leu Glu Met Val Pro Glu Lys
660 665 670
Arg Ala Ser Ala Gly Glu Cys Arg His Pro Trp Leu Asn Ser
675 680 685

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

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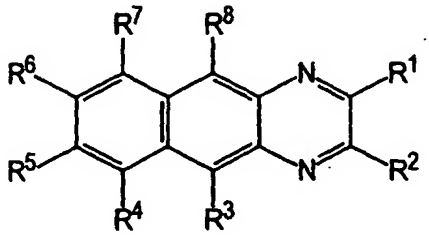
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: BENZO[G]QUINOXALINE DERIVATIVES AS EFFECTIVE COMPOUNDS AGAINST INFECTIOUS DISEASES



(I)

(57) Abstract: The present invention relates to benzo[g]quinoxaline derivatives of the general formula (I), processes for manufacturing said benzo[g]quinoxaline derivatives, the use of the benzo[g]quinoxaline derivatives as pharmaceutically active agents, especially for the prophylaxis and/or treatment of infectious diseases and opportunistic infections, diabetes, cancer, inflammation, as well as compositions containing at least one benzo[g]quinoxaline derivative and/or pharmaceutically acceptable salt thereof. Further, the present invention is directed to methods for preventing and/or treating of infectious diseases, diabetes, cancer, and inflammation using the inventive benzo[g]quinoxaline derivatives.

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INTERNATIONAL SEARCH REPORT

Inte... Application No
PCT/EP 02/05573

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D241/38 C07D403/14 C07D409/04 C07D401/14 C07D409/14
C07D405/14 C07D487/04 C07D403/12 C07D401/04 A61K31/517
A61P31/04 A61P31/12 C12Q1/48 C07K16/40 A61P31/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 115, no. 28, 1991 Columbus, Ohio, US; abstract no. 183362e, page 935; column 2; XP002230870 abstract & JP 00 374372 A (TERUMO CORP.) 28 March 1991 (1991-03-28) --- -/--	1,11, 34-37

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2003	04 07 2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	FRANCOIS, J

INTERNATIONAL SEARCH REPORT

Internat...pplication No
PCT/EP 02/05573

A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 130, no. 22, 1999 Columbus, Ohio, US; abstract no. 296316w, RODRIGO,G. ET AL.: "KINETICS STUDIES ON THE SYNTHESIS OF A SERIE OF 3-SUBSTITUTED QUINOXALINONES.COMPARISON WITH 3-SUBSTITUTED BENZOQUINOXALINONE" page 649; column 1; XP002230871 abstract & INF. TECNOL., vol. 10, no. 1, 1999, pages 29-35, BUENOS-AYRES ---	1,11, 34-37
X	WO 99 25327 A (WARNER-LAMBERT) 27 May 1999 (1999-05-27) page 27; claims ---	1,11, 19-21

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2003	

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	FRANCOIS, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/EP 02/05573

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 149 802 A (HOECHST) 31 July 1985 (1985-07-31) examples 51-54 ---	1,3,4
A	US 3 145 205 A (THOMAS OSDENE) 18 August 1964 (1964-08-18) column 1 -column 6 ---	1,11, 19-24
A	CHEMICAL ABSTRACTS, vol. 131, no. 24, 1999 Columbus, Ohio, US; abstract no. 317396k, EL ASHRY,ABDEL-RAHMAN: "SYNTHESIS AND ANTI-HEPATITIS B VIRUS ACTIVITY OF SOME 2,3-DIHYDROPROPYL UNNATURAL HETARYLS." page 33; column 1; XP002230872 abstract & ARCH. PHARM., vol. 332, no. 9, 1999, pages 327-30, WEINHEIM -----	1,11,19, 25,81,82

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/05573

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11,12,14-18,28-33,37,39,41-66,73 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-66,73,81,82

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-66,73,81,82

   Benzo[g]quinoxaline compounds and their pharmaceutical application.

2. Claims: 67-72,74-80

   Method for identifying compounds useful for the treatment of HBV infections and/ or diseases. Methods of regulating the production and/ or replication of HVB in human cells.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern_____ Application No
PCT/EP 02/05573

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 9925327 A2	27-05-1999
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US 3145205 A	18-08-1964	NONE	